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The European Journal of Pathology
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Aims and Scope
Mission statement: To advance the scientific basis of human pathology by the publication (encouragement and dissemination) of high quality research (including molecular and translational studies) and thereby contribute to patient care. Manuscripts of original studies reinforcing the evidence base of modern diagnostic pathology, using immunocytochemical, molecular and ultrastructural techniques, will be welcomed. In addition, papers on critical evaluation of diagnostic criteria but also broadsheets and guidelines with a solid evidence base will be considered. Consideration will also be given to reports of work in other fields relevant to the understanding of human pathology as well as manuscripts on the application of new methods and techniques in pathology. Submission of purely experimental articles is discouraged but manuscripts on experimental work applicable to diagnostic pathology are welcomed. Biomarker studies are welcomed but need to abide by strict rules (e.g. REMARK) of adequate sample size and relevant marker choice. Single marker studies on limited patient series without validated application will as a rule not be considered. Case reports will only be considered when they provide substantial new information with an impact on understanding disease or diagnostic practice.

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Abstracts

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OFP-02	Oral Free Paper Session Digestive Diseases Pathology – Liver/Pancreas
OFP-03	Oral Free Paper Session Joint Session: Autopsy Pathology / Cardiovascular Pathology / Pathology in Favour of Developing Countries / Electron Microscopy / Other Topics
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OFP-06	Oral Free Paper Session Paediatric and Placental Pathology
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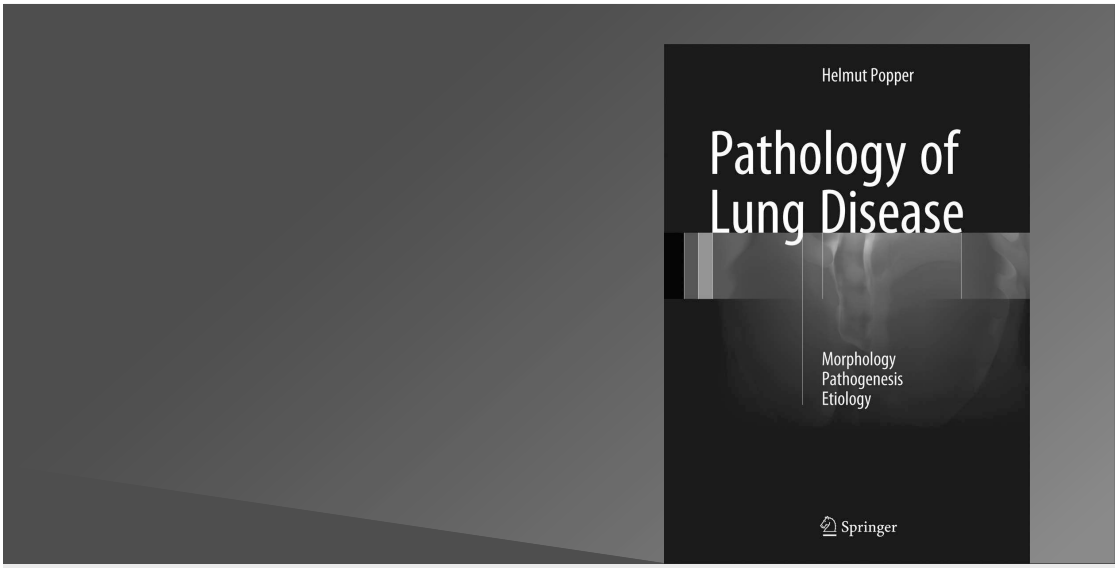

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Abstracts

29th European Congress of Pathology

Oral Free Paper Sessions

Sunday, 3 September 2017, 08:30–12:00, G109
OFP-01 Joint Session: Dermatopathology / Head and Neck Pathology

OFP-01-001
The role of R21 expression in differential diagnosis of melanocytic lesions
D. Turcan*, O. Pasaoglu
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Objective: R21 is a mouse monoclonal antibody directed against amino acids 203–216 of human soluble adenylyl cyclase protein. The aim of this study is to evaluate the usefulness of R21 expression in the differential diagnosis of melanocytic nevi (MN) and malignant melanomas (MM).
Method: R21 immunostaining was performed in 50 cases of MM (24 nodular melanomas, 9 superficial spreading melanomas, nine lentigo maligna melanomas, seven acral lentiginous melanomas, 1 unclassified) and 50 cases of MN (19 common melanocytic nevi, 19 dysplastic melanocytic nevi, 12 Spitz's nevi) diagnosed in our department between 2010 and 2016. Two different thresholds, 10 and 50 %, were used for positivity.
Results: The difference between these two entities was statistically significant for both cut-offs ($p < 0.001$). At the threshold of above 10 % R21-stained cells, the sensitivity was 72 %, specificity was 92 %, positive predictive value (PPV) was 90 % and negative predictive value (NPV) was 76 %. At the threshold of above 50 % R21-stained cells, the sensitivity was 60 %, specificity was 94 %, PPV was 90 % and NPV was 70 %.
Conclusion: Results of this study indicate R21 may have utility in the differential diagnosis of MM and MN.

OFP-01-002
PD-1 expression and its relation with histologic and clinical variables in mycosis fungoides
C. Vasquez*, C. Fumagalli, C. Pons, J. Muñoz, J. Szafranska, P. Garcia Muret, S. Novelli, A. Mozos
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Objective: Micosis Fungoides (MF) has an indolent evolution, and most cases have a prominent microenvironment. PD1 is expressed on activated T cells, interacts with its ligands and plays a role in microenvironment modulation. The aims of this study are to evaluate PD1 expression in MF cells, and to identify histologic variables that might have an impact on clinical outcome.
Method: 66 patients with MF were reviewed (37 males; 29 females, median follow-up:125 months (range 6–450 months). All cases were stained with PD1 (clone NAT105) and its expression was evaluated.
Results: MF cells express PD1 in a high proportion of cases (87.9 %). Only atypia, age >60 yo and advanced stage had an negative impact on overall survival ($p < 0.05$). Other histological variables, such as epidermotropism, tumour microenviroment and CD7 expression did not reach statistical significance. There was a weak correlation between atypia and proportion of cells with PD1 expression, PD1 intensity, and loss of CD7 expression ($r < 0.5$). The overall survival in the early stages was 85 % vs.64 % in advanced stages ($p < 0.05$).
Conclusion: In our series, we demonstrate a correlation between PD1 and atypia, and between atypia and overall survival. However, most of our cases expressed PD1, and therefore it might be a therapeutic target.

OFP-01-003
Up-regulation of FOXP1 in melanoma cells is a new unfavourable prognosticator and a specific predictor of lymphatic dissemination in cutaneous melanoma patients
P. Donizy*, J. Marczuk, K. Pagacz, W. Fendler, A. Halon, R. Matkowski
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Objective: To assess FOXP1 expression in tumour cells (TCs) and tumour-associated immune cells (TAICs) of 96 cutaneous melanomas, and analyze associations between FOXP1 expression and clinicopathological characteristics.
Method: An immunohistochemical analysis was performed for FOXP1 in 96 formalin-fixed paraffin-embedded primary cutaneous melanoma tissue specimens. The results were correlated with classical clinicopathological features and patient survival.
Results: Enhanced expression of FOXP1 in TCs was strongly associated with the presence of metastases in sentinel lymph nodes and positive status of regional lymph nodes. 96 % (52/54) of patients with low FOXP1 expression had no clinical or histopathological features of lymphatic dissemination. On the other hand, increased numbers of FOXP1-positive TAICs were observed in thinner and non-ulcerated tumours. Moreover, up-regulation of FOXP1 in TAICs was significantly associated with lack of regional lymph node metastases. Kaplan-Meier analysis revealed that high expression of FOXP1 in TCs was significantly correlated with shorter melanoma-associated overall survival and recurrence-free survival. FOXP1 expression in TAICs was not associated with clinical outcome. Multivariate analysis confirmed a significant impact of FOXP1 expression on unfavorable prognosis in melanoma patients.
Conclusion: Our results suggest that FOXP1 plays a key role in melanoma progression and is a potential target for molecular-based therapies.

OFP-01-004
Characterisation of the immunomodulatory effects of nivolumab and ipililumab in advanced melanoma by quantitative immunohistochemistry
R. Edwards*, J. Black, T. Young, F. Aeffner, J. Major, E. Neely, L. Cerkovnik, C. Mahrt, S. Kanaly, C. Horak, M. Montalto
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Objective: Understanding the mechanism of PD-1 checkpoint blockade will facilitate development of predictive biomarkers. We examined several immune markers from patients with advanced melanoma who did (IPI-T) or did not (IPI-N) receive ipilimumab prior to treatment with nivolumab (Checkmate CA209-038).

Method: Baseline and on-treatment (Day 29) biopsies (n = 54) were stained for CD8, PD-1, PD-L1, CD68, FoxP3 and CD4 by IHC. Digitized slides were subjected to image analysis (tIA, CellMap 0.8 software). Marker levels were compared using medians across the whole group, by ipilimumab subgroups and by BOR subgroups [responders (CR/PR), stable disease (SD), progressive disease (PD)]. Responses were assessed with RECISTv1.1.
Results: An increase was observed in all markers for the whole cohort, primarily driven by increases in Ipi-N; however, substantial increases were observed in CD8, PD-1 and PD-L1 in IPI-T responders. In the IPI-N subgroup, CD8, PD-1 and PD-L1 increased in PD and SD but did not change in responders. Both IPI-T and IPI-N subgroups showed higher baseline CD8, PD-1 and PD-L1 in responders vs SD and PD.
Conclusion: Patterns of immunomodulatory effect of nivolumab differ by ipilimumab pre-treatment. Further work is required to determine the significance of these differences and whether they underscore unique mechanisms of anti-tumour response.

OFP-01-005
Vascularised composite tissue allograft pathology: Akdeniz University experience
C. I. Bassorgun*, B. Unal, O. Dogan Ozkan, G. O. Elpek, O. Ozkan, M. A. Ciftcioglu
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Objective: Vascularized tissue allotransplantation differs from other solid tissue transplantations in that it involves several different tissues. Vascularized tissue allotransplantation pathology is important in detecting changes in the event of rejection. The histopathological examination for the detection of the rejection of vascularized tissue allotransplantation is generally based on the Banff 2007 classification.
Method: Routine skin biopsy specimens taken during the follow-up of seven patients were evaluated for rejection. Findings were rated according to the Banff 2007 classification. In a total of 96 biopsy specimens, findings of grade I mild rejection were observed intensively, while grade II moderate rejection was detected at secondary frequency.
Results: Besides the histopathological findings in the Banff 2007 classification, some additional histopathological findings were detected in our cases. The overlapping lesions were accompanied by drug eruption findings of rejection. In addition, although the cases showed high rates of grade I mild rejection findings contained in the Banff 2007 classification, no clinical evidence of acute rejection was detected.
Conclusion: We would like to present the findings that we observed during the routine histopathological examination of the five face transplant cases and two leg transplant cases performed by the Akdeniz University Plastic and Reconstructive Surgery Department.

OFP-01-006
The assessment of clinical and histopathologic effects of PUVA and NB-UVB in early stage mycosis fungoides
E. Yilmaz*
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Objective: Mycosis Fungoides (MF), the most common form of T-cell lymphoma, is staged as patchy, plaque and tumour forms. Although PUVA and narrow-band UVB (NB-UVB) are the two most commonly used treatment modalities in the early stages of disease, studies comparing their histopathologic effects are scarce. The aim of our study is to compare the clinical and histopathologic effects of PUVA and NB-UVB in early stage MF.
Method: The study included in 41 early stage MF cases treated with either PUVA or NB-UVB. Both clinical and histopathologic responses including the persistence of epidermotropism, changes in stratum corneum and epidermis, dermal infiltrates, dermal fibrosis and other dermal and vascular changes were evaluated. Complications during treatments were also noted.
Results: Complete clinical responses were seen in 14 of 23 patients (60.9 %) in the PUVA group and 11 of 18 patients (61.1 %) in the NB-UVB group. The two groups showed significant differences in terms of resolution of epidermotrophism, decrease in dermal infiltrates, and other dermal and vascular changes.
Conclusion: PUVA and NB-UVB have similar clinical and histopathologic effects in the treatment of early stage MF.

OFP-01-007
Tertiary lymphoid structures in ameloblastoma
C. H. Siar*, Z. A. Bin Abdul Rahman, H. Tsujigiwa, H. Nagatsuka, K. H. Ng
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Objective: The ameloblastoma is a benign but locally-invasive odontogenic epithelial tumour with a high recurrence rate after treatment. Tertiary lymphoid structures (TLS) are ectopic lymphoid formations representing an adaptive immune response to either specific pathogen, inflammatory challenge or neoplastic process. Although these structures are acknowledged measures of disease outcome in many cancer types, their role in ameloblastoma remains unclear. To address this, we investigated for their distribution, morphologic and immunophenotypic characteristics, and evaluated their relevance.
Method: Formalin-fixed paraffin-embedded specimens from 63 primary and 14 recurrent ameloblastoma cases were subjected to immunohistochemistry for expression of CD20, CD45RO, CD3, cortactin, NWASP, WIP, RANK, RANKL and osteoprotegerin. Intra- and peri-tumoural lymphocytic infiltrate, lymphoid aggregates and TLS findings were correlated with clinicopathologic parameters.
Results: There is a positive association between lymphocytic response with tumour status (primary versus recurrent). Peritumoural lymphocytic infiltrate, lymphoid aggregates and TLS were significantly higher in patients presenting with recurrent ameloblastoma ($P > 0.05$). Actin cytoskeletal regulators NWASP and WIP (except cortactin) overexpression within TLS and lymphoid aggregates suggests enhanced motility of T and B lymphocytes. A low RANK-RANKL and high osteoprotegerin profile within these lymphoid structures indicate an altered tumoural osteoimmunologic microenvironment.
Conclusion: Our results show that neogenesis of lymphoid organs do occur in ameloblastoma albeit in low frequency. Their enhanced presence in recurrent tumours may represent locally generated immune response with potential antitumour activity to control growth and progression.
(Grant: FP032-2015A)

OFP-01-008
Significances of androgen receptor (AR), Her-2, S-100P, Mammaglobin (MMG), AMACR expression in salivary pleomorphic adenoma (PA): Its relationship to the malignant potential in PA
K. Kusafuka*, T. Kawasaki, T. Nakajima, T. Sugino
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Objective: PA is the most common benign tumour of the salivary glands. Malignant change of PA is called "carcinoma ex pleomorphic adenoma (CXPA)", and its carcinomatous component frequently shows salivary duct carcinoma (SDC). We aimed to elucidate the malignant potential in PA.
Method: We selected PA (30 cases), atypical PA (APA: 5 cases), and CXPA (20 cases). We examined AR, GCDFP-15, Her-2, MMG, S-100P and AMACR expression, immunohistochemically.
Results: The inner ductal cells in PA were focally positive for AR, GCDFP-15, and S-100P, whereas they were very weakly and focally

positive or negative for Her-2. In this study, the carcinomatous component of CXPA was composed of SDC, most of which were strongly and/or diffusely positive for AR, GCDFP-15, Her-2, S-100P, MMG and AMACR. The inner cells of APA histologically had the large eosinophilic cytoplasm and nuclei with moderate atypia, and they were also positive for such markers.
Conclusion: According to AR and GCDFP-15 expression pattern, some inner cells of PA and APA have biologically malignant potential with apocrine differentiation, resembling the phenotype of SDC. The critical point of malignant change is the overexpression of Her-2 and/or S-100P, inducing aberrant MMG or AMACR expression.

OFP-01-009
Nasopharyngeal Carcinoma (NPC): Is there value in supplemental testing for EBV, p16 or HPV?
M. Hyrcza*, T. Thomson, C. Poh, J. Laskin, J. Siever, H. Yau, A. Jagdis, D. Hao
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Objective: Although NPC is associated with EBV, some cases instead show evidence of HPV. It is not clear if determination of EBV and HPV status in NPC is of clinical importance and should be routinely performed. We examined 143 NPC cases to determine the prevalence of EBV and HPV and their prognostic significance.
Method: Tissue microarrays were constructed and the cores were tested for EBV early RNA (EBER), p16 IHC and HPV RNA using in situ probes for high-risk HPV.
Results: Of the 143 cases , 133 were WHO Type III NPCs, 6 Type II, 1 Type I and 3 cores were missing. EBER was positive in 134 and p16 in 7 cases. Both were both positive in 5 cases. Among the 7 EBER- cases, 3 were p16+ and 4 negative. Three cases were positive for HPV RNA. The 5 year overall proportion surviving was 86 % (95 % CI = 79 %–90 %) with a median time at risk of 52 months (range 3 to 120 months). Disease-free survival at 5 years was 51 % (95 % CI = 42 %–59 %) with a median time at risk of 37 months (range 3 to 120 months). Combined EBER-/p16-negative cases had worse 2- and 5-year overall survival (p values 0.014 and 0.017 respectively). There were too few HPV-positive cases for outcome analysis.
Conclusion: In this cohort, HPV+ cases were rare (3 %) and not predicted by p16 testing. However, EBER-/p16- tumours had a worse prognosis, suggesting routine testing of EBER-negative cases for p16 may have prognostic utility.

OFP-01-010
Human papillomavirus-related carcinoma with adenoid cystic-like features: A series of 5 cases expanding the pathologic spectrum
J.-F. Hang*, M.-S. Hsieh, C.-C. Pan, Y.-J. Kuo
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Objective: Human papillomavirus (HPV)-related carcinoma with adenoid cystic-like features is a newly described entity of the sinonasal tract.
Method: We evaluated histomorphology, immunophenotype, and molecular testing of 5 HPV-related carcinomas with adenoid cystic-like features to identify potentially helpful features in distinguishing it from the classical adenoid cystic carcinoma (AdCC, $n = 14$) of sinonasal tract.
Results: Comparing to AdCC, HPV-related carcinomas with adenoid cystic-like features were associated with squamous dysplasia of surface epithelium (80 % vs 0 %, $P < 0.01$) and presence of solid growth pattern (100 % vs 29 %, $P = 0.01$), but less densely hyalinized tumour stroma (20 % vs 86 %, $P = 0.02$). Squamous differentiation in the invasive tumour was seen in 3 HPV-related carcinomas with adenoid cystic-like features, two of them showing abrupt keratinization and 1 with scattered squamous morules. Diffuse p16 staining in >50 % of tumour cells was noted in all HPV-related carcinomas with adenoid cystic-like features but only in 1 AdCC (100 % vs 7 %, $P < 0.01$). High-risk HPV testing was positive in all HPV-related carcinomas with adenoid cystic-like features (4 associated with type 33 and 1 type 16) but not AdCCs. MYB rearrangement was tested in 4 HPV-related carcinomas with adenoid cystic-like features and all showed negative.
Conclusion: We described novel pathologic findings of HPV-related carcinomas with adenoid cystic-like features, including squamous differentiation and association with HPV type 16. Diffuse p16 staining followed by HPV molecular testing is useful in distinguishing HPV-related carcinomas with adenoid cystic features from classical AdCCs.

OFP-01-011
Middle ear adenomatous neuroendocrine tumours: A 25-year experience at MD Anderson Cancer Center
D. Bell*, A. El-Naggar, P. Gidley
*MD Anderson Cancer Center, Dept. of Pathology, Houston, USA

Objective: Neuroendocrine tumours are uncommon in the head and neck region and extremely rare in the middle ear. Therefore, the clinical and pathologic characteristics of these tumours are less defined than neuroendocrine tumours of other sites. We reviewed our institutional experience with middle ear adenomatous neuroendocrine tumours (MEANTs).
Method: We searched our institution's pathology files to identify patients treated between 1990 and 2015 who had lesions classified as middle ear adenomas, adenomatous tumours, adenomatous tumours with neuroendocrine differentiation, carcinoid tumours of the middle ear, low-grade neuroendocrine tumours of the middle ear, and neuroendocrine carcinomas of the middle ear. When available, slides for the identified cases were retrieved and re-reviewed by two experienced head and neck pathologists (DB, AEN) to verify the histological diagnosis and exclude alternative diagnoses.
Results: We identified 14 patients (9 women and 5 men) age 29–65 years who received treatment for middle ear tumours at MD Anderson between 1990 and 2015. Although pathology slides were available for an additional 22 patients, no clinical follow-up data were available for these patients.
Conclusion: Our report adds to the series cases of MEANTs with recurrences, lymph node involvement, distant metastases, and tumour-related deaths. Our experience suggests that, although these tumours have long been considered to be low-aggression neoplasms, long-term follow-up studies to ascertain this supposed benignity are warranted. In conclusion, our institutional experience with MEANTs demonstrates that these tumours can recur, metastasize to the lymph nodes and distant sites, and cause death.

OFP-01-012
Clinicopathological study of ameloblastoma: An experiential status
H. Salam*, T. Mirza, M. Irshad
*Dow University of Health Sciences, Dept. of Oral Pathology, Karachi, Pakistan

Objective: With this experiential data, we aimed to identify the prevalent pattern for presentation of ameloblastoma in Pakistani population over 6 years of study period.
Method: All biopsy specimens diagnosed as ameloblastoma during the study period (January 2010–December 2015) were included in the study. The slides were reviewed and information pertaining to patient demographics, clinical presentation and tumour site was recorded on specifically designed proforma.
Results: Total 42 cases of ameloblastoma diagnosed during the entire study period. A wide age range (3 to 80 years) was observed with mean age 32 years at presentation. Highest incidence was recorded in 20–40 year age group. A slight male preponderance was noted (57 %).

Majority of the cases were intraosseous (76 %) amongst which mandible (87.5 %) was the most frequent site. An attempt was made to categorize all cases according to 2005 WHO classification, but due to fragmented biopsies, inadequate clinical and radiological correlation, a large percentage (40.5 %) of cases were classified as "uncategorized". Solid/multicystic variant was predominant (21.4 %).
Conclusion: Ameloblastoma is a rare neoplasm, a fact highligted by our recording only 42 biopsied cases over a span of 6 years. Even though the tumour has a predilection for higher age group and males, we recorded cases in both extremes of age. Therefore, ameloblastoma should be considered in differential diagnosis of odontogenic tumours at either extreme of age. Ameloblatoma has strong tendency for recurrence and recurrence rates vary for different variants. We emphasis the importance of adequate and accurate clinical information and radiographic correlation for proper categorization of this tumour.

OFP-01-013
TERT promoter region mutations in head and neck squamous cell carcinomas
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Objective: It is well known that head and neck squamous cell carcinomas are characterized by genetic alterations, instability and different immune defects and there are ongoing studies to find new mutations and its effective treatment modalities. Telomerase reverse transcriptase promoter (TERT) mutations have been reported in variety of tumours and often shown to be associated with aggressive behavior. The aim of the present study was to assess the prevalence of TERT promoter mutations in head and neck squamous cell carcinomas and correlate the results with patients' clinicopathological data.
Method: Total genomic DNAs of 213 head and neck squamous cell carcinomas were extracted from formalin-fixed paraffin embedded tissue samples. Mutations in the promoter region of the TERT gene (chr5, 1,295,228C>T/A and 1,295,250C>T) were analyzed using PCR-based direct sequencing method.
Results: Of 213 patients, 23 test samples were excluded from the study due to inadequate DNA quality. Of 190 patients with head and neck squamous cell carcinoma, TERT mutation was detected in 78 of 104 (75 %) oral cavity, 5 of 59 (8.4 %) larynx, 1 of 6 (16.6 %) hypopharynx and 0 of 21 (0 %) oropharynx locations. TERT promoter region mutations in patients with oral cavity carcinoma was higher than oropharynx, larynx and hypopharynx significantly ($p < 0.05$). Sequencing revealed that 65.4 % (51/78), 7.7 % (6/78) and 26.9 % (21/78) of oral cavity squamous cell carcinoma tumour tissues contained C228T, C228A and C250T mutations, respectively.
Conclusion: Oral cavity exhibits higher TERT promoter region mutations than other head and neck squamous cell carcinomas. It may play an important target for therapy and pathogenesis.

OFP-01-014
Diagnosis and characterisation of a new HPV-related tumour of the head and neck region
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Objective: We reviewed all sinonasal adenoidocystic carcinomas (ACC) previously diagnosed at our center to identify possible cases of the recently described HPV-related sinonasal carcinoma with ACC morphology
Method: p16 immunostain; high risk HPV DNA and mRNA in situ hybridization (ISH); HPV DNA amplification and genotyping. Patient follow-up data were reviewed.
Results: Fifteen ACC were diagnosed between 1994 and 2016, 9 in the nasal cavity and 6 in paranasal sinuses. Eight patients were males (53 %); mean age was 58 years (34–75). One high-grade, solid ACC from the nasal cavity of a 67 year-old female showed diffuse p16 and HPV mRNA ISH expression (6 %); LiPA SPF10 amplified HPV DNA but no specific genotypes; DNA ISH was negative. In all other cases, p16 stain was luminal and ISH negative; 3 were positive for HR HPV DNA. The tumour recurred 2 years after surgery and radiotherapy, and at 5 years the patient was alive with progressive disease. Three other patients (21 %) experienced tumour recurrence
Conclusion: HPV-mediated oncogenesis accounts for a small subset of sinonasal ACC. Diffuse p16 positivity with high-grade solid architecture requires confirmation with molecular tests, but PCR may be negative, even with prominent mRNA expression. The prognostic implications of this diagnosis are still need clarification.

OFP-01-015
Human papillomavirus in laryngeal lymphoepithelial carcinoma
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Objective: To investigate the involvement of Human papillomavirus (HPV) in Laryngeal Lymphoepithelial Carcinoma (LLEC).
Method: Four cases of LLEC were retrieved from our files from the period 2006–2016. Epstein-Barr virus (EBV) was tested in all cases with in situ hybridization with the INFORM EBER Probe (Ventana Medical Systems). Tissue was available for additional studies in three cases. P16 expression was analyzed with CINtec® p16 Histology (Ventana) and HPV DNA was tested through Polymerase Chain Reaction with SPF10 primers and INNO-LiPA HPV Genotyping Extra II (Innogenetics).
Results: All four cases were EBV negative. Three out of three cases were immunohistochemically p16 positive with an intense and diffuse pattern and were also positive for HPV-16 as detected by PCR. These results indicate that HPV was transcriptionally active in these cases.
Conclusion: Unlike nasopharyngeal carcinoma, LLEC is not related to EBV. The presence of transcriptionally active HPV suggests that it plays a role in LLEC.

Sunday, 3 September 2017, 17:15–19:15, G106-107
OFP-02 Digestive Diseases Pathology - Liver and Pancreas

OFP-02-001
Mutational landscapes of chemical hepatocarcinogenesis
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Objective: Hepatocellular carcinoma (HCC) shows molecular heterogeneity that reflects its diverse aetiology. Although next-generation sequencing of human liver tumours has defined recurrent mutations in HCC, few studies have compared these mutational landscapes to those present in commonly used mouse models of liver cancer.
Method: We used the well-established diethylnitrosamine (DEN) protocol to initiate liver tumours in 15-day-old C3H/HeOuJ mice, and collected spontaneous liver tumours arising in aged untreated C3H mice. Whole exome sequencing and histopathological analyses were performed in treatment-induced ($n = 50$) and spontaneous ($n = 25$) dysplastic nodules and HCCs.
Results: Exome-wide analyses of DEN-induced neoplasms revealed a high mutational burden of nonsynonymous single nucleotide variations. There were distinct mutational signatures in DEN-induced and spontaneous neoplasms although histopathologically they were indistinguishable. Activating Hras mutations were confirmed as the most common driver of DEN-induced hepatocarcinogenesis, followed by Egfr. Truncating Apc

mutations associated with aberrant nuclear beta-catenin expression were common in HCCs but not dysplastic nodules.
Conclusion: Here we show how the application of new sequencing technologies to traditional experimental models can reveal novel insights into the pathogenesis of liver cancer. Oncogenomic analyses are crucial for selecting the most appropriate preclinical mouse model for translational genetic, molecular, and/or histological studies.

OFP-02-002
Microbiopsies from pancreatic cysts—a novel approach to obtain a preoperative diagnosis
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Objective: To test if 1) it is possible to obtain a microbiopsy from a pancreatic cyst, 2) to make sure the microbiopsy offers sufficient tissue for histology, immunohistochemistry (IHC) and Next Generation Sequencing (NGS).
Method: Microbiopsies from pancreatic cystic lesions were performed on six patients referred for endoscopic ultrasound and fine needle aspiration, using the Moray microbiopsy forceps. The biopsies were processed for histology, and IHC staining for MUC1, MUC2, MUC6, MUC5AC, and CDX2. The cystic lesions were classified according to the WHO classification. Subsequent examination by NGS, using the Ion AmpliSeq Cancer Hotspot Panel v2 (Life Technologies), was performed.
Results: All patients had one or more adequate biopsies for histology, IHC, and NGS-analysis. All cases were classified as intraductal papillary mucinous neoplasia (IPMN) of pancreatobiliary subtype with low grade dysplasia. GNAS and concomitant KRAS mutations, specific of IPMN, were identified in two out of six cases. One patient had GNAS and BRAF mutation, and one patient had his initial endoscopic diagnosis of a pseudocyst changed to IPMN.
Conclusion: The microbiopsies offered adequate tissue for histology, IHC, and NGS-analysis, and contributed with additional diagnostic information with regards to subtype of IPMN, inclusive mutational profiling.

OFP-02-003
Mutant KRAS circulating tumour DNA as a biomarker for follow-up in patients with pancreatic adenocarcinoma
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Objective: Circulating tumour DNA (ctDNA) can be identified in the blood of cancer patients. The purpose of the study was to evaluate the usefulness of ctDNA analysis for follow-up of patients with pancreatic adenocarcinoma.
Method: Seventeen patients with pancreatic adenocarcinoma were included in the study. Blood samples were obtained during their routine follow-up visits and DNA was extracted from the cell-free component and scrutinized for low frequency KRAS mutations the Ion-Torrent PGM. KRAS mutant allele frequency was correlated with blood CA-19-9 levels and radiologic findings.
Results: Sixty eight samples were collected during 20 months follow up. The analytical sensitivity for calling KRAS mutations was 1 % mutant allele frequency. Seven (41 %) patients carried KRAS mutation in their plasma. Changes in KRAS mutant allele frequency correlated with radiological evaluation of disease status in eight of 12 (67 %) comparisons. Additionally, changes in KRAS mutant allele frequency correlated with plasma CA-19-9 levels in five out of nine (56 %) comparisons. In two cases ctDNA was a better predictor of disease status than CA-19-9.
Conclusion: KRAS ctDNA mutant allele frequency showed good correlation with both serological and radiological markers of disease status. Additionally, some results suggest that ctDNA might be a more accurate predictor of disease dynamics than CA-19-9.

OFP-02-004
Pathomolecular scoring and diagnostic algorithm of atypical hepatocellular adenomas: A clue for malignant transformation
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Objective: A subset of hepatocellular adenomas (HCA), called "atypical HCA" (a-HCA), show borderline features between HCA and hepatocellular carcinoma (HCC). This study aimed to evaluate the performance of a scoring system based on pathological (morphology, glutamine synthetase (GS) immunostaining pattern) and molecular (TERT promoter mutation) criteria to assess the risk of malignant transformation in a-HCA.
Method: Twenty resected hepatocellular tumours were classified by two pathologists as typical HCA (t-HCA) (n = 7), a-HCA (n = 6), HCA with obvious malignant transformation (HCA/HCC) (n = 5) and HCC (n = 2). In all HCA/HCC cases, the HCA component was classified as a-HCA. The pathomolecular scoring system (0–10) was based on the following criteria: cytonuclear atypias, pseudoglands formations, reticulin framework, GS pattern and non-tumoural liver aspect. TERT promoter mutations were determined by Sanger analysis in formalin-fixed and paraffin-embedded tissues.
Results: Median (range) pathomolecular score was 1 (1–2), 5.5(4–7), 7(6–9), 6.5(6–7) for t-HCA, a-HCA, HCA/HCC and HCC, respectively. High β-catenin activation (diffuse GS expression), was observed in none of the t-HCA, 3 (50 %) of the a-HCA, 4 (80 %) of the HCA/HCC and 1 (50 %) of HCC. Among a-HCA without obvious foci of HCC, none displayed TERT promoter mutations and all with high β-catenin activation had a score ≥6. TERT promoter mutations were only observed in 2(40 %) of HCA/HCC and 1(50 %) of HCC, all with a score ≥6.
Conclusion: These results suggest that a-HCA with a pathomolecular score ≥ 6 should be screened for TERT promoter mutations, suggestive of malignant transformation.

OFP-02-005
Immune microenvironment of pancreatic cancer (PDAC): The good, the "bud" and the "unusual" signature
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Objective: PDAC is a "non-immunogenic" neoplasm without significant response to immunotherapies. Our aim is to search for PDAC-subsets with higher amounts of intratumoural immune-cells and expression of immune-checkpoint molecules.
Method: Multipunch next-generation-tissue-microarrays from a well-characterized PDAC-cohort were immunostained for CD3, CD4, CD8 and CD20. Microsatellite-unstable tumours were excluded. An algorithm for digital image analysis was created. Immune-cells were counted in the intraepithelial and stromal compartment. Results were correlated with clinicopathologic features (TNM 8. Edition), tumour budding, presence of tertiary lymphoid tissue (TLT), PD-L1- and FOXP3-expression.
Results: In the tumour front adverse features correlated with reduced intraepithelial CD8- and stromal CD3- and CD20-counts. Immune signatures defined four PDAC-subgroups: a "quiescent", "T-cell-poor/B-cell-poor " group with aggressive features, high-grade budding and enrichment in FOXP3-Tregs; a "T-cell-rich/B-cell-rich-without-TLTs" group, associated with low-budding and better outcome; a "T-cell-rich/B-cell-rich-with TLTs" group, characterized by even less budding and the best outcome; and a "high (i.e. >25 %) PD-L1-expression" group, with "unusual" features (high-grade budding but favourable immune-microenvironment with high CD8- and reduced FOXP3-counts).

Conclusion: Simple immune signatures identify prognostically relevant PDAC-subgroups. B-cells are an essential element of the PDAC-microenvironment and their spatial organization is a key-regulator of their anti-tumour function. The relevance of the findings regarding immune-checkpoint inhibitors remains to be examined.

OFP-02-006

Long-term survivors with pancreatic ductal adenocarcinoma (PDAC) have lower p53 mutational burden and a favourable balance between tumour-associated and host-associated factors in the tumour microenvironment

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Objective: PDAC is a devastating disease with poor treatment response. Here we compare the mutational status and the T-cell composition in the tumour microenvironment (TME) between patients with long-term (>24 months) and shorter survival after surgical resection and adjuvant therapy

Method: Tissues from a well-characterized PDAC-cohort underwent next-generation sequencing (NGS) with a hot-spot cancer panel. The ratio CD8/Foxp3 (effector versus regulatory T-cells or Teff/Treg) was obtained. Results were correlated with clinicopathologic features (TNM 8. Edition), the presence of tertiary lymphoid tissue (TLT) and tumour budding.

Results: Long-term survivors showed a tendency for lower rate of p53 mutations ($p = 0.055$) and increased Teff/Treg ratio ($p = 0.0609$) along with significantly more frequent presence of tertiary lymphoid tissue ($p < 0.0001$) and lower tumour budding ($p = 0.0302$). TLTs and tumour budding were independent predictors of survival in the multivariate analysis including TNM-stage. No difference was observed concerning other common mutations (KRAS, ATM, EGFR, CDKN2A, PIK3CA, MET or GNAS) or the PD-L1 status.

Conclusion: p53 mutations are associated with tumour immune evasion and an unfavourable immune balance in the TME. Long-term survivors display a predominance of anti-tumoural immune responses, in correlation with low-budding and wild-type p53 phenotype. These parameters may help selecting PDAC-patients that would profit from an adjuvant or a neo-adjuvant approach.

OFP-02-007

Determination of nitrative and oxidative stress markers and the role of selective neutral sphingomyelinase inhibition in hepatic ischemia/reperfusion injury

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Objective: The aim of the present study is to determine the nitrative and oxidative stres markers folowing hepatic ischemia/reperfusion (IR) injury and to elucidate the effects of neutral sphingomyelinase (N-smase) inhibition in IR injury in liver.As known oxidative stres and nitric oxide (NO) production were reported in the pathogenesis of IR injury in some studies. NO production arises via nitric oxide synthase 2 (NOS2). N-smase/Ceramide pathway regulates the NOS2 expression.

Method: The rat model of hepatic IR injury was performed in our study. To create IR injury, the blood vessels sustaining median and left lateral lobes of liver were clemped for 60 min and followed reperfusion for 60 min. Nitrative and oxidative stres markers and the effects of N-smase inhibition were assesed according to several techniques (imunohistochemistry, mass spectrometric analysis, liquid chromatography, ELISA, histopathology etc.).

Results: NOS2 expression, protein nitration, nitrite/nitrate levels and sphingomyelin levels in liver tissue were elevated according to IR injury. Also, 4-hydroxynonenal (HNE) formation, protein carbonyl evels, xanthine oxidase (XO) transformation and ceramide levels were decreased according to N-smase inhbition.

Conclusion: This study is showed that nitrative and oxidative stress markers have a role in IR injury in liver and selective N-smase inhibition has a protective effect in IR injury.

OFP-02-008

Prognostic meaning of BAP1 and PBRM1 expression in intrahepatic cholangiocarcinoma

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Objective: Intrahepatic cholangiocarcinoma (iCC) has universally poor outcome, mainly due to its late clinical presentation. Identification of specific biomarkers and development of effective treatment are still urgently required. Mutations in PBRM1 and BAP1 genes have been related to survival in iCC patients. miR-31-5p seems also to play important regulatory functions in iCC and it directly regulates BAP1 expression in lung cancer. In this study, tissue expression of BAP1, PBRM1, and miR-31 was investigated in iCC and correlated with clinical-pathological features.

Method: Sixty-one consecutive patients who underwent curative hepatic resection for iCC were enrolled. None received any therapy prior to surgery. Immunostaining for BAP1 and PBRM1, and in situ hybridization for miR-31 were performed, using tissue microarray slides.

Results: A strong expression of BAP1 and PBRM1 was associated with a reduced overall survival ($p = 0.04$ and $p = 0.002$, respectively). Overexpression of PBRM1 was also related to a reduced disease-free survival ($p = 0.02$) and to perineural invasion ($p < 0.0001$). High levels of miR-31 were significantly associated to a low expression of BAP1 protein ($p = 0.01$).

Conclusion: In iCC, overexpression of BAP1 and PBRM1 is related to a poor prognosis and miR-31 may act as a direct regulator of BAP1.

OFP-02-009

Hepatitis E virus RNA and proteins in the human liver

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Objective: Hepatitis E constitutes a substantial disease burden worldwide. However, little is known about the localisation of hepatitis E virus (HEV) in the human liver. The aim of our study was to visualize HEV RNA and proteins in liver tissues.

Method: Twelve antibodies against HEV open reading frame (ORF) 1-3 proteins for immunohistochemistry (IHC) and two probes for in situ hybridization (ISH) were tested on formalin-fixed, paraffin-embedded (FFPE) Huh-7 cells transfected with HEV ORF1-3 expression vectors. IHC and ISH were then applied to HEV replicating human hepatoblastoma (Hep293TT) cells and to liver specimens from patients with hepatitis E ($n = 20$) and controls ($n = 134$).

Results: While ORF1-3 proteins were all detectable in HEV protein-expressing cells, only ORF2 and 3 proteins could be visualized in HEV-replicating cells. In liver specimens from patients with hepatitis E, only the ORF2-encoded capsid protein was unequivocally detectable. IHC for ORF2 protein showed a patchy expression in individual or grouped hepatocytes, generally stronger in cases of chronic compared to acute hepatitis.

In addition to cytoplasmic and canalicular, ORF2 protein also revealed a hitherto not described nuclear localisation. HEV RNA detection by ISH in defined areas correlated with positivity for ORF2 protein. IHC was specific and comparably sensitive as PCR for HEV RNA.
Conclusion: In livers from patients with hepatitis E, the ORF2 protein can be reliably visualized, allowing sensitive and specific detection of HEV in FFPE samples. Furthermore, its variable subcellular distribution in individual hepatocytes of the same liver might provide the basis for an interaction with nuclear components, and argues for a redistribution of ORF2 protein during infection.

OFP-02-010
Increased 53-binding protein 1 nuclear foci expression in the liver of patients with non-alcoholic fatty liver disease
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Objective: NA damage response (DDR) results in genomic instability, leading to transformation to cancer. However, presence of DDR in non-alcoholic fatty liver disease (NAFLD) is largely uninvestigated. We aimed to investigate the expression of 53BP-1 binding protein (53BP1), a DDR molecule that forms foci upon DNA double-strand breaks, in NAFLD.
Method: Forty paraffin-embedded human liver biopsy samples including five from normal livers, 10 from simple steatotic livers, and 25 from livers with non-alcoholic steatohepatitis (NASH) were studied by co-immunofluorescence with the anti-53BP1 and hepatocyte marker. Nuclear foci more than 2 were considered abnormal expression. Expression of 53BP1 was then compared with pathological features.
Results: The number of 53BP1 abnormal nuclear foci was significantly increased in the hepatocytes of NASH livers (30 %) and simple steatotic livers (20.1 %) compared to normal control (1.9 %). Expression of 53BP1 foci co-localized with that of histone 2AX, confirming the presence of DDR. The degree of 53BP1 abnormal expression was not significantly associated with NAS overall score but had positive correlation with lobular inflammation.
Conclusion: Our study suggests increased genomic instability in NAFLD liver, even when the routine pathological examination shows steatosis without NASH. Our finding may benefit the risk management of carcinoma occurrence in patients with NAFLD.

OFP-02-011
Hexokinase domain-containing protein (HKDC1) is overexpressed in and correlated with the histological progression of nonalcoholic fatty liver disease
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Objective: Nonalcoholic fatty liver disease (NAFLD) presents as either steatosis or steatohepatitis. Steatohepatitis is progressive, but its pathogenesis remains unclear. Hexokinase Domain Containing 1 (HKDC1) is a recently identified hexokinase-like gene, which functions as a hexokinase. Studies revealed that HKDC1 expression is associated with body fat deposition; however, its association with NAFLD has never been studied. The current study aims to explore HDCK1 expression in NAFLD in the context of disease progression.
Method: HKDC1 immunohistochemistry was performed on normal livers (n = 22) and liver with NAFLD (n = 26, 11 cases with advanced fibrosis). Immunostain intensity was graded as 0–1 (no or weak expression), 2 (moderate expression) and 3 (strong expression). Pearson's Chi-square test was used for statistical analysis.
Results: Normal hepatocytes have minimal HKDC1 expression. HKDC1 expression is significant increased in NAFLD characterized by strong expression in steatotic hepatocytes ($p < 0.001$). HKDC1 expression is further accentuated in steatohepatitis with hepatocyte ballooning ($p = p < 0.001$). Moreover, NAFLD with advanced fibrosis showed diffuse strong HKDC1 expression.
Conclusion: This is the first report showing increased HKDC1 expression in NAFLD. HKDC1 expression is positively correlated with the histological progression of NAFLD. Hepatic fat accumulation might be mediated by HKDC1; therefore, HKDC1 might be a potential target for treatment of NAFLD.

OFP-02-012
Genetic profile of pancreatic neuroendocrine neoplasms G3
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Objective: Pancreatic neuroendocrine tumours (PanNETs) G1-G2 usually show an intact TP53 and RB1 status. In contrast, neuroendocrine carcinomas (PanNECs G3) are commonly TP53 and/or RB1 mutated. Little is known about the genetic findings of NETs G3. In this study, we examined the genetic changes of NETs G3 and NECs G3 with the aim to define the genetic profile of these two tumour families.
Method: Tissue from 23 resected PanNENs, including 11 NETs G3 and 12 NECs, was examined by immunohistochemistry and next generation sequencing applying a 409 gene panel.
Results: NETs G3 harbored 49 mutations in 36 different genes, including MEN1 alterations in 5/11 cases. DAXX and TP53 were mutated in 1/11 cases each, ATRX and RB1 showed no alterations. NECs harbored 63 mutations in 44 different genes, including 8/12 TP53 and 5/12 KRAS mutations. Shared altered genes by NETs G3 and NECs were LRP1B (3/23), ARID1A (2/23), CDKN2A (2/23), APC (3/23) and TP53 (9/23). One NET G3 and two NECs did not show any mutations.
Conclusion: PanNETs G3 and PanNECs differ substantially in their genetic design. However, TP53 mutations may also occasionally occur in PanNETs G3.

Monday, 4 September 2017, 08:30–12:00, G109
OFP-03 Joint Session: Autopsy Pathology / Cardiovascular Pathology / Pathology in Favour of Developing Countries / Electron Microscopy / Other Topics

OFP-03-001
Reevaluation of clinical autopsies in the province of Vorarlberg/ Austria: A plea for diagnostic quality assessment in hospitals
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Objective: To detect discrepancies between clinical diagnoses and post-mortem autopsy diagnoses through reevaluation of clinical and autopsy records.
Method: Clinical and autopsy records of 897 autopsies performed in adults in 2005 (n = 325), 2010 (n = 293) and 2015 (n = 262) in Vorarlberg, Austria were retrospectively reviewed. The discrepancies between clinical diagnoses and autopsy diagnoses were classified according to Goldman criteria.
Results: Autopsy rates were decreasing between 2005 and 2015 (2005: 19,6 %; 2010: 14,6 %; 2015: 10,2 %) and were paralleled by an increase in major diagnostic errors (Goldman I + II). Therapeutically relevant errors (Goldman I) increased from 12,5 % to 15,5 % to 16,7 %. There was an increase of clinical underdiagnoses of neoplasms (2015: 2,5 %; 2010: 5,1 %; 2015: 9,9 %). Although the autopsy rate in cancer patients was relatively stable (2005: 13,4 %; 2010: 11,1 %; 2015: 11,3 %), the

number of unknown cancers confirmed only after autopsy tripled from 2005 to 2015 (1,7 to 4,6 %). No increase underdiagnoses was observed for pulmonary, cardiovascular, gastrointestinal and renal diseases.
Conclusion: The decreasing autopsy rate seems to be paralleled by an increase in clinical diagnostic errors, in particular overlooked neoplastic diseases. Performing autopsies in patients with unclear diagnoses remains an important tool for the diagnostic quality assessment in hospitals.

OFP-03-002
Unusual complete aortic arch and coronary occlusion with massive myocardial infarction after left-ventricular assist device thrombosis in a patient with heparin-induced thrombocytopenia
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Objective: An unusual autopsy finding in a 45-year-old woman with re-implantation of a left-ventricular assist device (LVAD) 6 months after removal of a LVAD.
Method: The patient received a second LVAD for progressive rapid heart failure 6 months after extraction of the previous device. Postoperatively acute LVAD failure was suspected, the transthoracic echocardiography revealed an aortic thrombus and an ejection fraction of 0 %. Subsequently the patient suffered cardiac arrest and all resuscitation attempts failed.
Results: The aortic arch was fully obstructed by a large thrombus with continuous blockage and thrombosis of all coronary arteries. Furthermore, numerous central and peripheral thromboemboli were found in both lungs. The left ventricular and septal myocardium showed signs of scarring and acute infarction. The previous LVAD aortic graft had been left in place without occlusion of its lumen. The patient had also developed a heparin-induced thrombocytopenia (HIT) after removal of the first LVAD, leading to distribution of thromboemboli as well as a continuous thrombosis from the old graft, with full aortic arch and coronary obstruction.
Conclusion: LVAD thrombosis is associated with substantial morbidity and mortality and the already elevated risk of thrombosis is multiplied by the added risk of thromboembolic complications associated with HIT. Therefore, the practice of leaving the graft in place, especially without occlusion of it lumen, should be re-evaluated in cases of patients with coagulopathies.

OFP-03-003
Retrospective evaluation of congenital heart defects in fetal autopsies and comparison with prenatal ultrasound
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Objective: Congenital heart defects (CHD) are the most common structural defects in newborns. This study pretend to demonstrate cardiac autopsy anomalies and evaluate concordance between prenatal ultrasound and postmortem findings (PU/PF).
Method: Retrospective review of 1372 fetal autopsies performed at Centro Hospitalar e Universitário de Coimbra between 2005 and 2016. For evaluation of CHD were established 13 categories for classification prenatal ultrasound and autopsy findings and posterior correlation. Statistical analysis was performed by Cohen test.
Results: 223 fetuses were included in this study, 114 males and 109 females. The median maternal age was 34 years (range 16–47) and gestational age 21 weeks (range 12–37). The most common pathologies were ventricular septal defect (25.56 %), complex cardiopathy (20.62 %) and auriculo-ventricular septal defect (13 %). Excluding 84 cases without ultrasound description, there was moderate agreement between prenatal ultrasound and postmortem findings, with Kappa = 0,434 (95 % Confidence Interval, 0,350-0,518), $p < 0{,}0005$.
Conclusion: Moderate agreement between PU/PF in fetuses with CHD seems acceptable because this study encompassed a broad spectrum of defects, some of them difficult to evaluate by ultrasound such as small ventricular septal defects. The commonest cardiac anomaly was ventricular septal defect, in agreement with other studies. Nevertheless second most common defect, complex cardiopathy, represents a higher proportion than described in literature.

OFP-03-004
Rare chromosomopathies and cardiac anomalies in fetal autopsies
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Objective: The main objective of this study was to evaluate the spectrum of cardiac anomalies found in rare chromosomopathies in routinely performed fetal autopsies.
Method: A retrospective study of fetal autopsies was performed between 2005 and 2016. We identified the main cardiac anomaly presented in the selected group and divided in 7 major groups (Trissomy 21, 18, 13, 9, Monossomy X, Triploidy and Structural anomalies). Structural chromosomic anomalies were analysed.
Results: In the selected period, a total of 1,372 fetal autopsies were performed. Cardiac anomalies were identified in 223 cases, from which 126 (56.5 %) presented with chromosomopathies. The most common was Trisomy 21 identified in 68 (54.0 %) fetuses. The least common, found in 9 (7.1 %) cases, were structural anomalies: del22q11.2 [x3]; 46,XX, t(1;6)(p22.1;q25.1) [x2]; 46,XY der(18) t(11;18); 46,XX, der(14;21)(q10;q10) + 21; 48,XYY dup22; 46,XX dup3. The most common cardiac anomaly was ventricular septal defect and complex anomalies, each presented in 3 (33.3 %) cases. All pregnancies were submitted to elective termination of pregnancy.
Conclusion: Chromossomopathies are one of the most common causes of congenital cardiac anomalies. Structural anomalies are rare and can also be associated with cardiac anomalies, thus the importance of the correct description of these cases for future reference.

OFP-03-005
Clinical postmortem CT can demonstrate the cause of death or guide the autopsy
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Objective: To investigate the potential of postmortem CT (pmCT) to improve the clinical diagnosis of cause of death.
Method: 86 cadavers underwent whole-body pmCT before conventional autopsy (CA). Radiologists and pathologists were blinded to each other's results and compiled their own reports. Differences in the number of correctly identified clinical diagnoses, prior and post pmCT, as to cause of death, type of pathology and anatomical system involved, were investigated by use of McNemar tests, with autopsy as the reference standard.
Results: Using pmCT, the number of correctly identified causes of death, type of pathology and anatomical system involved increased from 53 to 64 % ($p = 0.05$), from 65 to 83 % ($p = 0.001$) and from 65 to 84 % ($p = 0.001$) respectively. The subgroup of cardiovascular causes of death showed almost the lowest sensitivity (54 %) for cause of death after pmCT, but the most significant increase in sensitivity for anatomical system, from 62 to 82 % ($p = 0.02$) using pmCT.
Conclusion: pmCT significantly improves clinical diagnosis as to the cause of death. If the exact cause of death is uncertain after pmCT, radiologists can indicate a particular region of interest, directing pathologists,

which in turn may be able to reduce the invasiveness of a conventional autopsy.

OFP-03-006

Netosis in coronary plaque ruptures, plaque erosions and intraplaque hemorrhages of myocardial infarction patients at autopsy

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Objective: Netosis is a form of cell death characterized by formation of neutrophil extracellular traps (NETs). To evaluate its participation in coronary atherothrombosis, we investigated the presence and distribution of NETs in coronary plaque ruptures, plaque erosions and intraplaque hemorrhages (IPHs).
Method: Forty-four coronary plaques were retrieved at autopsies from 36 myocardial infarction patients, of which, in HE-stains, were classified as 9 erosions, 18 ruptures and 17 IPHs. 20 intact plaques were selected as controls. Thrombus material in plaques was graded as either fresh, lytic or organized. Immunohistochemistry was performed to visualize neutrophils (MPO) and NETs (citrullinated histone-3/CitH3 and PAD4). Results of immunostaining were scored semi-quantitatively.
Results: Neutrophils (MPO+) and NETs (CitH3+ and PAD4+) were abundantly present in all types of complicated plaques, with no significant differences in extent between ruptures, erosions and IPHs. NETs were found in the thrombus, the underlying plaque tissue and adventitia, the latter with the highest amount in eroded plaques. Fresh and lytic thrombi contained significantly higher numbers of neutrophils and NETs than organized thrombi. In contrast, intact plaques contained no neutrophils and NETs.
Conclusion: Netosis takes part in all distinct types of atherothrombosis, with presumed role in thrombus progression towards vessel occlusion.

OFP-03-007

Balances of different types of cell death in coronary thrombus in relation to thrombus age and instability, after myocardial infarction

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Objective: Fragile thrombus (instability) is associated with a higher mortality rate after acute myocardial infarction (AMI). We investigated which types of cell death are present and involved in thrombus stabilization, over time.
Method: Coronary thrombosuction aspirates of AMI patients were histologically classified in HE-stains as fresh (15), lytic (13) or early organizing (8). An immunohistochemical sequential triple staining was performed using anti-C-reactive protein (necrosis), anti-caspase-3 (apoptosis) and anti-citrullinated histone H3 (ETosis) as primary antibodies. For each specimen, the presence and most prominent type of cell death were semi-quantatively recorded and presented as a percentage of total observations.
Results: All 3 types of cell death were found to be present in all 3 age categories. The most prominent types of cell death observed in fresh and lytic thrombi were ETosis (44.9 and 40 % of specimens, respectively) and apoptosis (43.6 and 35.7 %, respectively), followed by necrosis (11.5 and 24.3 %, respectively). ETosis appeared the most prominent type of cell death found in organizing thrombi (40 % of specimens), but in these thrombi necrosis (37.5 %) was more dominant than apoptosis (22.2 %).
Conclusion: Cell death, along several pathways, is a prominent mechanism in thrombus tissue of AMI patients, and can lead to thrombus instability / fragility.

OFP-03-008

New formula for cardiothoracic ratio for the diagnostic of cardiomegaly on post-mortem CT

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Objective: The cardiothoracic ratio (CTR) is considered to be a reliable detector of cardiomegaly on the CT for livings. Our study aimed to establish an adjusted CTR based score to predict cardiomegaly at post-mortem computed tomography (PMCT).
Method: We selected adult's autopsy cases between 2009 and 2016. Two groups (normal heart weight and overweighed heart) were considered. The CTR was measured on axial images. Logistic regression analysis was performed to investigate the discriminating power of the CTR between groups when adjusting to the confounding factors.
Results: 120 cases with normal heart weight and 100 cases with overweighed heart were analyzed. The factors associated to the cardiomegaly are CTR (p-value = 0.003, OR = 3.57), BMI (p-value = 0.055, OR = 1.09), age (p-value <0.001, OR = 1.67) and gender (p-value 0.002, OR = 4.85). An integer-based point-scoring system was derived based on their β-Coefficients. The score ranged from 21 to 45 with highest values indicating a more likely cardiomegaly. For a threshold of 33, the sensitivity, specificity and the correctly classified were 0.84, 0.78 and 0.81 respectively.
Conclusion: CTR alone cannot be used to discriminate between normal heart weight and overweighed heart at PMCT. A new formula has been developed, including age, gender and BMI to diagnose the cardiomegaly at PMCT.

OFP-03-009

Extra-pulmonary tuberculosis in Nepal: A tip of an iceberg

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Objective: Tuberculosis is a common condition in the underdeveloped countries like Nepal annual case notification rate (CNR) is 136 per 100,000 populations. Tuberculosis is the 6th leading cause of death in Nepal. Tuberculosis is a preventable disease if diagnosed in time. Extra Pulmonary Tuberculosis is 23.1 % out of total registered Tuberculosis cases in the country. Therefore, objective of this study is to determine the Extra Pulmonary Tuberculosis (EPTB) pattern in the specimen received in pathology lab that may help to understand the prevalence and disease identification.
Method: Pathology Lab Database analysis of Histo-cytology specimens for Extra Pulmonary Tuberculosis during 5 years period from 2011 to 2016 at PAHS, Kathmandu, Nepal.
Results: Out of approximately 20,000 specimens received in the Pathology Department in the 5 year period 1 % was of Extra Pulmonary Tuberculosis (EPTB). Lymph nodes comprised of 58 %, followed by Gastrointestinal and Skin in 10 each and 8 % cases were seen in the urogenital tract.
Conclusion: This study represents facility based data only; so it may reflect the tip of an iceberg of at risk population who dwell in the rural mountainous area where the diagnostic facility are not available. Merely the clinical judgement should not overlook the probability of Extra Pulmonary Tuberculosis.

OFP-03-010

Introducing MiniTEM for ultrastructural pathology

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Objective: MiniTEM is a desk-top transmission electron microscopy and analysis platform with a high degree of automation in the microscope

operation, image acquisition and analysis process. The system is comprised of a low-voltage (25 keV) transmission electron microscope and software combining microscopy operation and analysis. It requires only a single wall socket and runs in a standard lab. In this study we show that MiniTEM produces images of sufficient quality for ultrastructural analysis and diagnosis.
Method: Samples were prepared by standard methods (embedded in resin, sectioned in a microtome in 50–100 nm sections, and post-stained). The samples were then imaged and analyzed in the MiniTEM system using the automatic alignment procedures, autofocus, and auto illumination functionality.
Results: Clinical samples of various disorders were analysed in MiniTEM (e.g. para crystal inclusions (muscle); Systemic Lupus Erythematosus (SLE) (kidney), and Primary Ciliary Dyskinesia (PCD) (cilia). The image quality and resolution provided was evaluated by experts.
Conclusion: The image quality and resolution offered in MiniTEM is sufficient for ultrastructural diagnostic purposes. The ease of use and high degree of automation offered in MiniTEM reduces many of the hurdles associated with conventional TEM and can hence make TEM information more accessible.

OFP-03-011
Autophagy in advanced gastric adenocarcinomas of intestinal type: An ultrastructural investigation
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Objective: Electron microscopy has been considered the gold-standard method to reveal autophagy, a dynamic process fundamental for the turnover of cellular organelles. Enhanced autophagy has been reported in hypoxic areas of solid tumours; however, there are only few ultrastructural reports concerning the relationship between autophagy and tumour grade.
Method: We have performed an ultrastructural investigation aimed to document autophagy in 25 cases of advanced gastric adenocarcinomas intestinal type, twelve of which were well differentiated and thirteen poorly differentiated.
Results: Autophagic changes were only occasionally found in well-differentiated carcinomas, while they constitute a frequent ultrastructural finding in poorly differentiated ones. These changes represent a peculiar feature in undifferentiated phenotype together with rare organelles, numerous microfilaments, prominent nucleoli, heterogeneous or plurilobated nuclei and micronuclei.
Conclusion: On the light of our observations, it can be argued that autophagy is not constantly present in all intestinal type gastric adenocarcinomas, but it seems to be a phenomenon related to the tumour progression and differentiation.

OFP-03-012
A call for unified guidelines on pathology reporting
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Objective: To compare different guidelines for pathology reporting of colorectal cancer (CRC) used around the world and to underline the importance of creating unified guidelines.
Method: We have investigated the guidelines for reporting CRC surgical specimen of: The College of American Pathologists, The Royal College of Pathologists, The Royal College of Pathologists of Australasia and the Polish Society of Pathology. We have conducted a survey among pathologists from different European countries to find out what guidelines they follow in their routine practice and how they are being followed.
Results: Significant differences exist between colorectal cancer guidelines of major pathology societies. Universal guidelines would facilitate the workflow and enable a more effective cooperation between different countries. It would make it easier to interpret the pathology report from any country especially in therapeutic trials. It would benefit the patients, as they would be ensured with an equal diagnosis and therefore treatment choice independently of the country of origin.
Conclusion: We present the advantages as well as the disadvantages of the unification of the guidelines and the differences between major guidelines. There are pros and cons to the approach of creating universal guidelines, however in our opinion, it would be beneficial.

OFP-03-013
Codeposition of apolipoprotein A-4 with amyloid protein of systemic and localised types
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Objective: Amyloid proteins consist of main primary proteins and codeposition proteins such as SAP, ApoE, and ApoA1. To date, apolipoprotein A4 (apoA4) were found in many amyloid proteins by mass spectrometry-based proteomics (Vrana 2014). However, in cardiac amyloidosis apoA4 was found separately with wild-type transthyretin (Bergstrom 2004). The aim of this study is to investigate the association of apolipoprotein A-4 with amyloidogenesis.
Method: We purified amyloid fibrils from systemic and localized amyloidosis, separated their constituents by PAGE, and identified amyloid specific proteins by mass spectrometry. With anti-apoA4 antibody, many different types of amyloid deposits were stained.
Results: By mass spectrometry, apoA4 proteins were found in systemic and localized amyloidosis (3/3) cases. By immunostaining, amyloid deposits of AA(5/6), AL(systemic9/11, localized4/4), AB2microglobulin(2/2), Senile(1/1) Aortic valve (3/3) were positive for anti apoA4. Light chain deposition diseases were negative (0/2). Positive areas were coincident with Congo-red positive amyloid deposits.
Conclusion: ApoA4 were codeposited with many different kinds of amyloid proteins and should be a cofactor for amyloid fibril formation. Anti ApoA4 may be available for detecting amyloid deposits.

OFP-03-014
Comparing digital pathology with standard optical microscopy in diagnostics: A large multicenter, retrospective non-inferiority study in 2,000 surgical pathology cases
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Objective: In one of the largest studies of its type, this study was designed to demonstrate that diagnosing surgical pathology slides with a digital pathology platform (Philips Intellisite Pathology Solution (PIPS)) was non-inferior to using an optical microscope. Secondary objectives included comparison of digital and optical discordance rates for organs, subtypes and pathologists.
Method: A non-inferiority study design was used to compare optical vs digital reads of 2000 surgical pathology cases from 20 different organ systems (54 subtypes) with 16 reading pathologists from 4 institutions, resulting in 16,000 reads. In order for the digital method to be declared non-inferior to the optical method, an error rate of less than 4 % was set as the target for the upper bound of the 95 % two-sided confidence interval for the optical-digital rate difference.
Results: A total of 1992 cases were included in the Full Analyses Set with 15,925 readings. The study determined a digital major discordance rate of

4.7 %, an optical major discordance rate of 4.4 %, and a digital-optical rate difference of 0.4 with a 95 % confidence interval of (0.30 %; 1.01 %).
Conclusion: This study demonstrates that viewing, reviewing and diagnosing surgical pathology tissue slides by using the Philips Digital Pathology Solution is non-inferior compared to optical microscopy.

OFP-03-015
Development of a "Patient Harm Index" to quantify adverse events in anatomic pathology: An effective motivator towards high reliability and error reduction?
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Objective: To describe the development of a novel patient-centric metric for measuring adverse events in anatomic pathology (AP).
Method: As part of an institution-wide quality improvement project, service lines (SL) developed lists of preventable adverse events to aim for reduction. The sum of such adverse events in each SL represented their Patient Harm Index (PHI). Historic data were used to develop threshold/target/reach goals.
Results: Cases with one of following events resulting in patient harm or potential harm constituted the AP PHI: (1) major diagnostic error, (2) major frozen section (FS) discrepancy due to sampling, (3) major FS discrepancy due to interpretation, (4) significant/unexpected finding without documented communication in report and (5) significant diagnostic delay, specimen loss, or results reported on wrong patient. 48 (4 % reduction), 45 (10 % reduction) and 40 (20 % reduction) were set as threshold, target and reach goals, respectively. Progress towards these goals was discussed at faculty, staff and quality management meetings. By year-end, 38 patients had potential/adverse events. This 24 % reduction in the potential/adverse event rate (0.061 to 0.046 %) appeared more meaningful when translated into 12 less patients with potential/adverse events.
Conclusion: By aggregating the total number of potential/adverse events in time and supplementing other, more traditional "rate-based" metrics, the PHI emphasizes the numerator and deemphasizes the denominator, keeping the focus on the patient rather than the total number of specimens. We believe that this, along with being able to add up all events together into a single more comprehensible number, provide greater motivation for error reduction.

Monday, 4 September 2017, 14:45–16:45, G109
OFP-04 Gynaecological Pathology

OFP-04-001
The differential diagnosis of cervical adenosquamous carcinoma (CAC) and related entities
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Objective: Although the WHO 2014 criteria require the presence of unequivocal glandular and squamous differentiation, CAC in practice represent a diverse spectrum of lesions, some of which do not exhibit unequivocal squamous differentiation.
Method: Full slide sets from 61 CAC (including glassy cell and related lesions), invasive carcinomas resembling "stratified mucin-producing intraepithelial lesion" (invasive SMILE) and usual-type adenocarcinomas with squamous metaplasia were collected from 7 institutions worldwide. CAC was diagnosed only when unequivocal malignant glandular and squamous differentiation was present. This pattern was distinguished from 3 lesions: 1) Usual-type adenocarcinoma with benign-appearing squamous metaplasia; 2) Glassy cell carcinoma; 3) Invasive SMILE (Schoolmeester and Lastra). TMAs were constructed and immunohistochemistry for p16, p63, vimentin and PR was performed on 44 cases. Endometrial adenocarcinomas involving cervix were excluded.
Results: Of the 61 CACs and related lesions classified by 2014 WHO, 32 CAC cases remained, while 9 were reclassified as pure invasive SMILE, 4 as mucinous adenocarcinoma with invasive SMILE, 7 as usual-type adenocarcinoma with invasive SMILE, 6 as usual-type adenocarcinoma with benign-appearing squamous metaplasia and 1 as poorly differentiated usual-type adenocarcinoma. 2 glassy cell carcinomas remained. The vast majority of the CACs and reclassified cases were p16+ and, while none were vimentin+. 60 % of CACs represented in the TMA were p63+, while only 1/20 reclassified cases were positive. Results for other markers were tabulated.
Conclusion: The differential diagnosis of CAC includes one new entity, usual type adenocarcinoma with squamous metaplasia, and a newly described lesion, invasive SMILE. P63 should be used to verify the presence of squamous differentiation (when malignant) to ascertain a diagnosis of CAC. Study of the clinical significance of these lesions is ongoing.

OFP-04-002
Histological grading of cervical intraepithelial neoplasia (CIN) in colposcopically directed punch biopsies: Audit and assessment of CIN1-2 terminology and its impact on patient management
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Objective: Aiming for 100 % adherence to the three-tier grading system (CIN1, 2 and 3), audit use of CIN1-2 terminology in cervical biopsies, assessing potential overtreatment of low-grade lesions by large loop excision of the transformation zone (LLETZ) procedures.
Method: In-depth analysis of all cervical punch biopsies with CIN1-2 diagnosis over a 3-year period. Data collected using the electronic patient record included colposcopic findings, reporting pathologist, and all subsequent cervical histology with grade of dysplasia and use of p16 immunohistochemistry recorded.
Results: 95.15 % adherence to three-tier grading system. 87/4458 (1.95 %) biopsies reported CIN1-2. 61/87 subsequent LLETZ procedures showed: 2/61 HPV changes, 10/61 CIN1, 5/61 CIN1-2, 29/61 CIN2, 10/61 CIN2-3 and 5/61 CIN3. Biopsy reported CIN1-2 had low- and high-grade dysplasia on subsequent LLETZ specimens in 10/61 and 44/61 cases respectively. 12/4458 (0.27 %) low-grade lesions were potentially overtreated.
Conclusion: CIN1-2 Is infrequently reported and overtreatment of low-grade lesions (HPV changes & CIN1) rare. 72.1 % of biopsies reporting CIN1-2 showed high-grade dysplasia (CIN2 & 3) on subsequent LLETZ specimens. Block p16 immunostaining can be a useful diagnostic adjunct when high-grade dysplasia is suspected. We recommend avoiding the use of CIN1-2 terminology, especially as patient management is based on a two-tier (low- and high-grade dysplasia) grading system.

OFP-04-003
Invasive stratified mucin-producing carcinoma (SMPC): A study in morphology, immunohistochemistry and Human papillomavirus (HPV) status
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Objective: To describe the morphology, immunohistochemical profile and HPV status in stratified mucin-producing carcinoma (SMPC), an

endocervical adenocarcinoma (EAC) that is the invasive counterpart to stratified mucin-producing intraepithelial lesion (SMILE).
Method: 21 SMPC were collected from 7 institutions, diagnosed as destructively invasive tumours composed of cells with mucin stratified throughout its entire thickness. Other associated patterns—usual, mucinous and adenosquamous carcinoma were recorded. TMAs were constructed and immunohistochemistry for several markers were performed on 12 cases (7 pure, 5 mixed) (see Table 1). HPV in-situ hybridization was performed using the ACD RNAscope® system (7 pure cases).
Results: Of the 21 SMPC, 9 were pure while 12 were associated with other histologic subtypes: 6 usual, 3 adenosquamous, 3 mucinous. All tested cases were positive for HPV (7/7) while 8/12 were diffusely positive for p16 and only 2/7 were PAX8 positive. Two cases showed p53 null pattern (aberrant). The remaining IHC results are shown in Table 1. Table 1 POSITIVE HPV ISH (7/7) 100 % P16 (8/12) 67 % CA-IX (4/7) 57 % MUC6 (4/7) 57 % PAX8 (2/7) 29 % P40 (2/7) 29 % PR (3/12) 25 % HNF1beta (1/7)14 % GATA 3 (1/7)14 % P63 (1/11) 9 % Vimentin (1/12) 8 % Her2 (1/12 2+) 8 % NEGATIVE SATB2 HIK1083 AR CDX2 *p53 (2/11) 18 % *null expression
Conclusion: SMPC is a morphologic variant of EAC that can occur in pure form or be associated with usual, adenosquamous or mucinous carcinoma. These are HPV associated tumours with a distinct morphology and similar immunoprofile as usual adenocarcinoma. Notably SMPC can be negative for PAX8.

OFP-04-004
Correlation between immunoexpression of ARID1A, PD-L1, mismatch repair proteins and microsatellite instability in ovarian clear cell carcinomas
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Objective: Mismatch-repair (MMR) status predicts for response to immune checkpoint inhibitors in colorectal cancers. Ovarian clear cell carcinomas (OCCC) can demonstrate MMR defects and often show ARID1A loss. We assessed the relationship between immunoexpression of ARID1A, PD-L1, MMR proteins and microsatellite instability (MSI) in these tumours.
Method: Immunohistochemistry for ARID1A, PD-L1 (SP142, Spring Bioscience), MLH1, MSH2, MSH6 and PMS2 was performed on 103 OCCC. MSI status was assessed. Extent of PD-L1 membranous staining in the tumour and peritumoural immune component was scored.
Results: 18(17 %) OCCC stained for PD-L1 and 6 showed ≥30 % positivity. 57(55 %) tumours exhibited peritumoural immune PD-L1 staining. Five and 3 tumours showed abnormal MMR expression [MLH1/PMS2(2), MSH2/MSH6(1), MSH6(2)] and MSI-H, respectively. Two PD-L1 expressing tumours (both showing ≥30 % staining) have abnormal MMR/MSI-H. All OCCC with abnormal MMR/MSI-H demonstrated peritumoural immune PD-L1 staining. 35(34 %) OCCC showed ARID1A loss, of which 7 and 21 showed tumoural and peritumoural immune PD-L1 staining, respectively. Overall, there is no correlation between MMR deficiency ($p = 0.174$) or ARID1A loss ($p = 0.628$) with PD-L1 tumoural expression.
Conclusion: Tumour and peritumoural immune PD- L1 expression in OCCC is not associated with MMR deficiency or ARID1A loss. Further studies are needed to assess the therapeutic utility of PD-L1 inhibitors in these tumours.

OFP-04-005
Technical and interpretive performance characteristics of p53 immunostaining: British Association of Gynaecological Pathologists (BAGP) and United Kingdom National External Quality Assessment Service (UKNEQAS) collaborative project
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Objective: To determine technical and interpretive performance characteristics of p53 immunostaining
Method: Sections from a tissue microarray of 42 tubo-ovarian carcinomas with known TP53 mutation status were stained for p53 by 37 laboratories. 96 pathologists/biomedical scientists (range 1-7 /laboratory) interpreted these staining results independently as normal (wild-type), abnormal (mutation-type), or uninterpretable. Slides from 32 laboratories were returned for central review.
Results: Excluding uninterpretable results on central review, 24 of 32 laboratories had either complete agreement with the reference value or a single discrepant result (>95 % agreement); in three laboratories there was disagreement with the reference value for two cores, while the five remaining laboratories showed disagreement for 3 to 10 cores, with the main problem being poor sensitivity in detection of abnormal p53 expression (sensitivity: 0.36–0.77). Absolute agreement in interpretation of p53 staining between local and central opinion was 89 %. Most disagreements were between abnormal (complete loss) and uninterpretable in the absence of an internal control.
Conclusion: Performance characteristics of p53 technical staining quality are excellent for most participating laboratories, with 0-2/42 discrepant staining results. A minority of laboratories ($n = 5$) experienced significant problems in staining quality, leading to false negative results. There was substantial but improvable inter-observer agreement in p53 interpretation.

OFP-04-006
Utility of GATA3, TTF1 and PAX8 in identifying mesonephric carcinomas of the gynaecologic tract
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Objective: It has recently been reported that GATA3 and TTF1 are useful markers for identifying mesonephric carcinomas of the gynecologic tract. Our goal was to determine the sensitivity and specificity of GATA3/TTF1 for mesonephric carcinomas using a broad series of uterine carcinomas.
Method: Using tissue microarrays and/or whole sections, we assessed the immunohistochemical expression of GATA3, TTF1 and PAX8 in a series of 604 uterine carcinomas. Any intensity of staining in >1 % of cells was considered positive.
Results: GATA3 distinguished mesonephric carcinoma from other uterine carcinomas ($p < 0.0001$), but TTF1 did not ($p = 0.42$). GATA3 had a sensitivity of 85 % and specificity of 93 %. GATA3 was also positive in 18 % of carcinosarcomas (carcinoma and/or sarcoma component) and was seen in carcinosarcomas with squamous metaplasia. The proportion of GATA3 positive cells decreased as the mesonephric carcinomas became more poorly differentiated. All 7 mesonephric carcinomas were PAX8 positive. Ninety-four percent of cases overall were PAX8 positive; 4 cases were PAX8 negative and GATA3 positive.
Conclusion: Although GATA3 is a sensitive and specific marker for mesonephric carcinomas, it also stains a subset of carcinosarcomas. A very small proportion (0.6 %) of all cases were GATA3 positive and PAX8 negative, overlapping with the immunoprofile of breast carcinomas.

OFP-04-007
Combined ASRGL1 and p53 immunohistochemistry as an independent predictor of survival in endometrioid endometrial adenocarcinoma
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Objective: The prognostication of endometrial cancer is based on clinicopathological risk factors and a systematic analysis of a prognostic

immunopanel is lacking. We evaluated whether an immunopanel could reliably assess endometrioid endometrial cancer (EEC) outcome independent of clinicopathological information.
Method: A cohort of 306 EEC specimens was profiled using tissue microarrays (TMA). Immunohistochemical analysis of well-established tissue biomarkers (ER, PR, HER2, Ki-67, MLH1 and p53) and two new biomarkers (L1CAM and ASRGL1) was carried out. Statistical modeling with embedded variable selection was applied on the staining results to identify minimal prognostic panels with maximal prognostic accuracy.
Results: A panel including p53 and ASRGL1 immunohistochemistry was identified as the most accurate predictor of relapse-free and disease-specific survival. With this panel, patients were allocated into high- (5.9 %), intermediate- (29.5 %) and low- (64.6 %) risk groups. Cases in the high-risk group (aberrant p53, low ASRGL1) had a 30-fold risk ($p < 0.001$) of dying of EEC compared to low-risk group. The statistical modeling favored p53 over L1CAM for prognostic role in EEC.
Conclusion: P53 and ASRGL1 immunoprofiling stratifies of EEC patients into three risk groups with significantly different outcomes. This easily applicable panel could be a useful tool in EEC risk stratification and guiding the allocation of treatment modalities.

OFP-04-008
Expression of DNA methyltransferases in ovarian tumours
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Objective: DNA methylation is responsible for gene silencing in various tumour types and is mediated by five DNA methyltransferases (DNMT1, 2, 3a, 3b, 3 L). The purpose of the present study was to explore the expression of DNMTs in borderline and malignant ovarian tumours.
Method: We examined the expression of DNMT1, DNMT2, DNMT3a and DNMT3b in 72 serous (12 borderline tumours, 15 low-grade carcinomas, 45 high-grade carcinomas) and 19 mucinous (12 borderline tumours, 7 carcinomas) primary neoplasms and in 16 relapsed serous carcinomas by immunohistochemistry. Nuclear staining was evaluated for all markers. Cytoplasmic staining was additionally evaluated for DNMT2 and DNMT3a. Intensity of staining (1–3) was multiplied by the % of positive cells. Mann-Whitney and Wilcoxon signed-rank tests were used for statistical analysis.
Results: DNMT1 expression was increased in high-grade compared to low-grade serous carcinomas and in relapsed tumours compared to their primaries ($p < 0.001$ and $p = 0.007$, respectively). Cytoplasmic expression of DNMT3a was lower and nuclear DT3α expression was higher in high-grade compared to low-grade serous carcinomas ($p = 0.04$ and $p = 0.004$, respectively). DNMT2 and DNMT3b expression did not show any correlation with tumour type or relapse.
Conclusion: Our results suggest a possible involvement of DNMT1 and DNMT3a in the pathogenesis and progression of high-grade serous carcinomas.

OFP-04-009
Upfront pathology review in the randomised PORTEC-3 trial for high risk endometrial cancer
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Objective: In the PORTEC-3 trial, patients with high-risk endometrial cancer (HREC) were randomised to receive pelvic radiotherapy with or without concurrent and adjuvant chemotherapy. The aim of this analysis was to evaluate the role of expert pathology review before randomisation.
Method: Six hundred eighty-six HREC patients were included in the PORTEC-3 trial; 184 (27 %) in the United Kingdom and 145 (21 %) in the Netherlands. A total of 1295 cases underwent central pathology review, of whom 1226/1295 (95 %) had available matching review and original reports. Inter-observer agreement was evaluated by the kappa value (κ).
Results: Among the 1226 potentially eligible patients, 6356 selected pathology items were evaluable for both original and review pathology. In 43.4 % of patients at least one pathology item changed after review. In 102 patients (8.3 %), this discrepancy led to ineligibility for the PORTEC-3 trial, most frequently due to differences in the assessment of histological type (34 %), endocervical stromal involvement (27 %) and histological grade (19 %).
Conclusion: Central pathology review by expert gynaecological pathologists changed histological type, grade or other items in 43.4 % of HREC patients, leading to ineligibility for the PORTEC-3 trial in 8.3 %. Upfront pathology review is essential to ensure enrolment of the target trial-population, and to avoid over- or undertreatment.

OFP-04-010
Test p16/Ki67 twice-positivity and colposcopy with biopsy first-negativity: Detecting histologic HSIL-risk women in 12–18 months follow-up
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Objective: Current secondary cervical cancer prevention algorithms have limitations in detecting cancer precursors. p16/Ki67 test with simultaneous co-expression of anti-proliferative and proliferative proteins has been proposed as a biomarker of high-grade cervical intraepithelial lesions. We investigated whether twice-positive p16/Ki67 test—in first testing and in follow-up—will improve identification of these.
Method: 8350 automated proceeded LBC, including 1952 cotesting, have been performed in primary cervical cancer screening. Immunocytochemical p16/Ki67 double staining was done in 347 cases using automated preparation system. 181 women with ASC-H or higher or ASC-US/LSIL cytology and HPV-positive were referred to colposcopy with biopsy. 24 patients with histological LSIL or less (biopsy first-negativity), reached follow-up cotesting with p16/Ki67 test and biopsy in 12–18 months.
Results: Diagnostic value of twice-positive p16/Ki67 for histologic HSIL (hHSIL) for the second follow-up biopsy was evaluated. Follow-up p16/Ki67 was positive in 10 women – 8 hHSIL and 2 hLSIL cases were diagnosed in biopsy. 1 hHSIL was p16-Ki67 twice-negative. Sensitivity/specificity/PPV/NPV of p16/Ki67 for hHSIL in the second biopsy were 89/86/80/93 (CI 95 %) respectively.
Conclusion: Twice-positive p16/Ki67 test can be a precise biomarker in triage patients for hHSIL-risk groups. Also, it might be decisive in referring to 12–18-month follow-up biopsy without prior cytology or HPV testing.

OFP-04-011
Overexpression of SOX 9 protein in endometrial carcinoma
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Objective: Endometrial carcinoma is the most common gynecological malignancy in developed countries and the carcinogenesis is not fully understood. SOX 9 is a transcription factor involved in the tumourigenesis of a number of cancers, however its role in endometrial carcinoma is uncertain. This study is to examine the

SOX 9 expression in normal endometrium and endometrial carcinoma.
Method: Immunostain of SOX 9 was performed in 32 cases of endometrial carcinoma and 30 cases of benign endometrium. Stains of Sox 9 were scored as weak (no staining 0, weak staining 1+) and strong (Stains 2+ and 3+) nuclear staining and results were interpreted by two pathologists.
Results: The expression of Sox 9 was only identified in nuclei of endometrial glandular epithelium and not in endometrial stroma. Over expression of Sox 9 is identified in majority of endometrial carcinoma 66 % (21/32) while the staining pattern of Sox 9 is weak or none in majority of normal endometrium. Only 19 % (6/31) of normal endometrium has strong but focal nuclear staining ($p = 0.0003$).
Conclusion: This study shows significant overexpression of SOX 9 protein in nuclei of endometrial carcinoma compared to normal endometrium. This overexpression may play a role in the carcinogenesis of endometrial carcinoma.

OFP-04-012
Differentiating primary pulmonary squamous cell carcinoma from squamous cell carcinoma of the cervix metastatic to the lung: Histological and immunohistochemistry study
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Objective: Distinction between primary and metastatic pulmonary squamous cell carcinoma(SCC) is difficult. We aimed to define histological and immunohistochemical features helpful for the differential diagnosis of pulmonary SCC metastases originating from the cervix.
Method: Retrospective review of primary pulmonary SCC($n = 22$) and lung metastases from cervix SCC($n = 21$) diagnosed at IPO-Porto(1995–2017). Clinicopathological data was retrieved and histological features were re-evaluated. Immunohistochemistry study with ER, PR, TTF-1, p63, and CK7 was performed. Statistical analysis was done to compare groups.
Results: Compared to patients with primary pulmonary SCC, those with cervix SCC lung metastases were younger(mean age: 54 years vs. 69 years) and more frequently presented with multinodular disease(31% vs. 14 %). Median time between primary cervical SCC and lung metastasis was 30 months. Histologically, cervix SCC lung metastases predominantly featured large regular nests with moderate cytological atypia, while primary lung SCC often presented small irregular nests with severe atypia. Keratinization was more frequent in cervix SCC metastases(60% vs. 32 %). Immunostaining showed diffuse p63 and absence of TTF-1, ER and PR expression in all cases. CK7 was more often positive(76% vs. 64 %), with stronger and more diffuse staining in metastatic SCC(median Allred-score:7vs.4).
Conclusion: An integrated approach, comprising clinical, histological and immunohistochemical features, is essential for the differential diagnosis between primary and metastatic SCC originating from the cervix.

Monday, 4 September 2017, 17:15–19:15, G106-107
OFP-05 IT in Pathology

OFP-05-001
Template based synoptic reporting improves oncological pathology reports regarding data content and clarity of data layout
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Objective: Traditionally, pathology reports have been textual with a high degree of variability. In part, they miss some of the information needed for e.g. therapy decision. Here, we describe a TNM-adapted toolset including a PIS-integrated structured template that contributes to improving pathology reports of prostate, lung, and breast resection specimens.
Method: Pathology reports of oncological prostate ($n = 1049$), lung ($N = 878$) and breast ($n = 4181$) resection specimens were classified into descriptive reports (DR), structured reports (SR), and template based synoptic reports (TBSR). The report types were compared regarding the content of organ specific essential data, summarized in an essential data score (EDS), and regarding the time a gynecologist needed to detect all essential data within a subset of breast specimens reports.
Results: All 11 ED of prostatectomy specimens were included in 2.7 % of DR, 43.5 % of SR and 97.2 % of TBSR with a statistically highly significant difference ($p < 0.0001$). A high-score EDS of 10 was measured in 2.6 % of DR of lung resection specimens, 16.4 % of SR, and 88.4 % of TBSR ($p < 0.0001$). Regarding reports of breast resection specimens a full-score EDS of 9 was seen in 4 % of DRs, in 21.4 % of SRs, and in 72.3 % of TBSRs ($p < 0.0001$). Mean data detection time decreased significantly from 26 to 20 and 14 s in DRs, SRs, and TBSRs, respectively.
Conclusion: Structuring improve the quality of pathology reports reflected by an increased content of essential data and a high clarity of data layout resulting in a rapid detection of essential data by clinicians.

OFP-05-002
Automatic cell detection in the bone marrow by a convolutional neural network-based approach
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Objective: Automatic detection of cells is an important step for the analysis of tissue composition and spatial arrangement. Partially overlapping cell nuclei (either two are erroneously detected as one or one bizarre configured is detected as two) are one major challenge, which we intend to address by a convolutional-neural network based cell segmentation approach.
Method: The approach is implemented in MATLAB with the free-available convolutional neuronal network toolbox MatConvNet (www.vlfeat.org/matconvnet/).
Results: The detection process can be divided into several steps: i) By applying a sliding window the input image is decomposed into many small tiles. ii) These tiles are analyzed by a convolutional network (pre-trained to classify the tile content) leading to a tile-wise probability value for containing one single cell. iii) To take different cell-sizes into account, the steps i and ii are repeated with sliding windows of different sizes. iv) To avoid double-detection and to optimize the bounding box a combination of non-maxima-suppression and a second convolutional network (pre-trained to classify the deviation of the box size and position) is applied.
Conclusion: The results will be compared to manual segmentation and its robustness against image variations (e.g. illumination changes) will be the objective of ongoing investigations.

OFP-05-003
Feasibility of real-time digital pathology by the Panoptiq™ imaging system compared with conventional light microscopy in diagnosing cervicovaginal cytology cases
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Objective: Digital pathology has been increasingly gaining the attention of pathologists worldwide. However, the application of digital cytology is relatively unexplored. The Panoptiq™ imaging system enables the operator to combine low-power panoramic digital images with high-power Z-stacks of regions of interest with a significantly smaller image size than that obtained by whole slide scanning. This study aimed to evaluate the

efficiency of the Panoptiq™ imaging system in digital cytology in comparison with the conventional light microscope in assessing cervicovaginal cytology specimens.
Method: One hundred liquid-based cytology slides were selected sequentially. The cases were reviewed by a pathologist and a cytotechnologist by using conventional light microscopy and digital cytology, based on the Bethesda classification system. The Cohen's kappa coefficient was calculated to measure the agreement between both modalities.
Results: Case distribution was as follows: normal and atypical, 33/100; intraepithelial lesions, 60/100; and malignant, 7/100. Digital cytology showed an inter-modality agreement of 0.83 to 0.85, indicating minor non-inferiority of digital image-based diagnosis compared to microscopy. The overall experience of the observers was satisfactory, and some reported that the digital cytology image allowed more detailed observation than the light microscopy image.
Conclusion: The Panoptiq™ imaging system is feasible while ensuring diagnostic accuracy.

OFP-05-004
Validation of diagnosing melanocytic lesions on whole slide images—does z-stack scanning improve diagnostic accuracy?
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Objective: We aim to establish the diagnostic accuracy of whole slide imaging (WSI) for melanocytic lesions and study the potential accuracy increase of using z-stack scanning. Z-stack enables pathologists to use a software focus adjustment, comparable to the fine-focus knob of optical microscopy.
Method: Melanocytic lesions (n = 102) were selected from the Pathology archive: 35 benign, 5 Spitzoid tumour of unknown malignant potential (STUMP) and 62 malignant lesions. Nine of the malignant cases comprised nevoid melanoma. All glass slides were scanned using 40× objective in z-stack mode (seven levels with 0,6 micrometer interval). A ground truth diagnosis was established on the glass slides by four academic dermatopathologists. Next, six non-academic surgical pathologists subspecialized in dermatopathology read the WSI.
Results: An expert consensus diagnosis was achieved in 99 (97 %) of the cases. Concordance rates between surgical pathologists and the ground truth varied between 69 and 89 %. Pathologists used the software focusing option in 7–28 % of cases. Concordance rates of nevoid melanoma varied between 11 and 89 %. Z-stack didn't improve diagnostic accuracy of melanocytic lesions.
Conclusion: Large variability in diagnostic accuracy of melanocytic lesions exists, which may partly be caused by use of WSI. Z-stack scanning does not increase diagnostic accuracy of melanocytic lesions.

OFP-05-005
Tumour proportion scoring of programmed death-ligand 1 positive cells using digital image analysis
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Objective: To investigate the diagnostic capability of digital image analysis for assessing programmed death-ligand 1 (PD-L1) protein expression in histological specimens of non-small cell lung cancer (NSCLC).
Method: Digital images of histological specimens stained with PD-L1 IHC 22C3 pharmDx were imported into a database and tumour regions-of-interest (ROIs) were outlined. PD-L1 positive membranes and cell nuclei were identified using a series of polynomial filtering methods. The total number of tumour cells were quantified and a Tumour Proportion Score (TPS) was calculated from the number of PD-L1 positive and negative tumour cells.
Results: The PD-L1 image analysis application consistently identified negative tumour cells and cells showing complete or partial membrane staining at any intensity on samples ranging from 0 to at least 50 % TPS assessment by pathologists. Out of 10 tissue microarray cores stained by 6 different laboratories, 83.33 % of the cases were in agreement with manual scoring. One core manually scored as negative was consistently found to have more than 1 % PD-L1 staining, causing 10 % of the errors.
Conclusion: Quantitative digital pathology was shown to accurately quantify and score PD-L1 stained tumour cells in NSCLC tissue samples. The automation and large-scale analysis potential of the application could become a powerful tool for pathologists.

OFP-05-006
Discriminating between ductal carcinoma in situ and invasive tumour components using digital image analysis
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Objective: To investigate, with a digital image analysis (DIA) system, the importance of discriminating between ductal carcinoma in-situ (DCIS) and invasive tumour components (ITC) when using tissue-based biomarkers for diagnosing breast cancer.
Method: Digital images of serial whole tissue sections, one double-stained with CK7/19 and p63 and the other stained with the analytical marker Ki-67 or HER2, were aligned using the VirtualDoubleStaining™ technique. Using novel Visiopharm image analysis algorithms ITC regions were identified based on the CK7/19 stain and DCIS regions were identified based on the joint CK7/19 and p63 stain. These regions were transferred to the analytical slide, where the biomarker expression was quantitated within the ITC regions only or within the ITC regions and the DCIS regions. The two set of results were compared to manual scores.
Results: The presented DIA system has been found to robustly discriminate between DCIS and ITC facilitating the quantification of biomarker expression within ITC only. Preliminary results show that this could improve the diagnostic capabilities when using tissue-based biomarkers for diagnosing breast cancer.
Conclusion: Using DIA to reliably detect and eliminate DCIS components from the consecutive analysis of biomarker expression could prove to be an important tool when diagnosing breast cancer using tissue-based biomarkers.

OFP-05-007
Importance of hot spot definition for Ki-67 quantification using digital image analysis
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Objective: Assessment of biomarker expression in automatically identified hot spots rather than manually assessed hot spot or as an average of the entire tumour area is currently being discussed and implemented into scoring guidelines, but a consistent definition of hot spots has not yet been defined. In this analytical study we investigate the influence of the way the hot spot is defined and the consequences it has on the quantification of Ki-67.
Method: Digital images of serial whole tissue sections, stained with pan-CK and Ki-67 respectively, were aligned using the Visipharm VirtualDoubleStaining™ technique. The pan-CK image was used to separate the tumour component from the stromal tissue, and restrict the remaining analysis to tumour regions. Ki-67 positive and negative nuclei were identified and a heatmap was generated. Based on this heatmap four types of hot spots were created: circle, square, heat map count and heat map area. For each hot spot type the adjustable parameters where varied to assess the impact of the hot spot definition on the Ki-67 quantification.
Results: Ki-67 scores on analytical samples as a function of the hot spot definition.

Conclusion: Proper application of hot spot definition can significantly affect the Ki-67 proliferation index in clinically relevant samples.

OFP-05-008

An investigation into tumour cell counting on hematoxylin and eosin stained tissue specimens

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Objective: In routine pathological practice the percentage of tumour cells is estimated by pathologists on Hematoxylin and Eosin (H&E) slides, this has been shown to be unreliable. Many studies have compared the manual counting of cells from small regions to the pathologist estimation. It however necessary to extend this to whole slide estimation of cell count where a validated cell identification will provide information on decision making and also provide a ground truth for algorithmic identification.
Method: 25 lung cases were retrieved and regions of tumour were identified by a pathologist (independent) and annotated. Three pathologists were asked to assess each of these regions for tumour percentage. Additionally, the region inside these annotations had an optimized threshold applied to identify the nuclei. A classifier was trained using cellular specific features (densitometric/morphological) to allow the classification of nuclei into the two categories of Tumour/Non-Tumour.
Results: The plot of ground true against the pathologist estimation show a R2 value 0.27. 8 % where accurate, 17 % of cases being under estimated. Seventy-five percent of all cases were overestimated.
Conclusion: Pathologists generally over-estimated tumour content. This is due to an underestimation of non-tumour cells. Optimized cell count and classification provides an effective ground truth to tumour cell counting.

OFP-05-009

Qualitopix—automatic quality assessment

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Objective: Objective: Staining sufficiency in immunohistochemistry (IHC) is essential for patient diagnostics. Therefore, proficiency testing should be performed by External Quality Assessment (EQA) organizations using expert pathologists. We propose to use digital image analysis for automatic quality assessment, to assist pathologists and to assure an objective assessment.
Method: Methods: Image analysis can be used to extract useful information from a virtual IHC slide. The useful information with respect to quality assessment is e.g., completeness of membrane staining (assessing human epidermal growth factor receptor 2 [HER 2]) [1] or percentage and intensity of tumour nuclei staining (assessing estrogen receptor [ER]). Our image analysis method captures completeness of membrane staining using connectivity [2] and percentage and intensity of tumour nuclei staining using H-score [3].
Results: Results: A Receiver Operating Characteristic (ROC) analysis of the quality assessments performed by pathologists from NordiQC and our automatic method reveal an area under the curve of 0.98 for HER2 assessments and 0.93 for ER assessments. The assessments were classified into sufficient and insufficient.
Conclusion: Conclusion: Our image analysis method shows promising results for automatic quality assessment of both HER2 and ER, rendering the method useful as a support for EQA organizations or as an objective quality assessment for individual laboratories. [1] RA Walker et al., "HER2 testing in the UK: further update to recommendations," Journal of Clinical Pathology, 2008. [2] A Brügmann et al., "Digital image analysis of membrane connectivity is a robust," Breast Cancer Res Treat, 2011. [3] NL Andersen et al., "A Digital Approach to Immunohistochemical Quantification of Estrogen Receptor Protein in Breast Carcinoma Specimens," Appl Immunohistochem Mol Morphol, 2017.

OFP-05-010

The evolution of the microscope; digital pathology as a means of enhancing patient care

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Objective: The microscope has been the mainstay tool of pathology practice for well over a century. Our institution has made a commitment to incorporating newer digital microscopy technologies and we intend to show how it has enabled pathology practice and patient care.
Method: We illustrate our various digitization processes including glass slide scanning for clinical archival, live streaming telecytology, and robotic microscopy. We will discuss the consequential changes in operations, culture and care delivery. This high level of digitization has also enabled our efforts in computational pathology.
Results: Glass slide digitization is over 200,000 glass slides per year with plans to scale up to 500,000 glass slides per year. All rapid on-site fine needle adequacy evaluations (ROSE FNAs) are now performed through telecytology. Close to 7000 ROSE FNAs per year are through live streaming telecytology and 500 ROSE FNAs per year are through robotic telemicroscopy. Enabled by the wealth of digitized imaging data, computer assisted diagnostic tools are currently under development.
Conclusion: Incorporation of digital technologies has been transformative, allowing us to disseminate expertise and enhance patient services. Moreover, because of our immense resource of imaging data, we are able to apply machine learning efforts to propel further pathology practice.

OFP-05-011

PIE: The Dutch Pathology Image Exchange platform for diagnostics and panels

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Objective: Digital exchange between pathology laboratories of whole slide images (WSI) for consultations, revisions and panels enables an efficient diagnostic process reducing time before patients can start treatment. The Dutch Pathology Image Exchange (PIE) project aims to create a nationwide platform for WSI exchange securing privacy by employing the PALGA infrastructure.
Method: In a pilot manual and automated upload of WSI is developed in laboratories representing a variety of providers of scanners and viewers. Panels are also selected on the basis of frequency of meetings. The pilot serves as a blueprint for other laboratories and panels.
Results: The number of revisions and consultations in The Netherlands is estimated at 40,000, the number of patients discussed in panels at 6,000. The current process may take up to 2 weeks before a patient receives the final diagnosis. PIE may reduce this process to a few hours to one or 2 days only depending on the availability of the consulting pathologist.
Conclusion: After the pilot PIE will be open for participation to all Dutch laboratories. Using PIE patients with complex diagnoses requiring consultation or revision will no longer experience unnecessary delay in treatment. This unique effort may serve as example for similar initiatives worldwide.

OFP-05-012

Validated interhospital digital pathology (whole slide imaging) / telepathology practice in a multi-institutional health group in Turkey

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Objective: Whole slide imaging, converts an entire slide into a digital image that allows seeing in a computer screen all slide instead of a chosen area. WSI has been performed in Acibadem University the department of Pathology since 2013 for routine histopathologic & cytopathologic diagnosis. We conducted a validation study regarding the use of WSI based on an institutional experience.
Method: Two experienced pathologists were enrolled for the study. One pathologist was located in Ankara, and the other worked in various AHG locations. The digital slide scanner used was either Pannoramic Flash 250 or Pannoramic Midi from 3DHISTECH. They examined the glass slides then reviewed their former report to note if there were any differences in their previous diagnoses. The cases were classified as agreement, disagreement-minor and disagreement-major. For disagreements, pathologists were asked to describe the reason(s) for it.
Results: Result for pathologist 1: Agreement between digital and paraffin was 94.8 %. The 5.2 % disagreement was mostly (4.2 %) due to failure to detect rare H. Pylori microorganisms. If H.pylori is not considered than the agreement would be 99 %. Result for pathologist 2: The difference between digital versus paraffin diagnoses is 2,1 %. Agreement is 97.9 %.
Conclusion: One software adjustment may not fit for all. Routine pathology sign-out sessions (including frozen sections, IHC, FISH, BDISH) may be performed securely with virtual slides. However more validation studies might be necessary since the spectrum of pathology specimens is very wide.

Monday, 4 September 2017, 17:15–19:15, D203
OFP-06 Paediatric and Perinatal Pathology

OFP-06-001
P57 immunostaining pattern of complete mole in Lagos University Teaching Hospital
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Objective: P57 immunohistochemistry has been proven as a veritable ancillary technique in diagnosis of molar pregnancy especially in differentiating between partial and complete mole (CM). CM does not express the staining because p57 is paternally imprinted and maternally expressed. This study is aimed at highlighting the p57 staining pattern amongst CM diagnosed in our institution
Method: Formalin Fixed Paraffin Embedded sections from archived blocks (2008–2014) were made for p57 immnuohistochemistry using auto immunostaining processing according to DAKO guidelines. The staining waas referred as adequate with positive internal control (decidua, extravillous trophoblasts) or external control (normal products of conception). The staining pattern of the cytotrophoblast nuclei and stroma villus cells were recorded
Results: One hundred percent of the CM stained negatively for p57 with 75 % having positive internal control. Twenty-five percent of the cases had no internal control staining positive, however the external control in the batches were positively stained. The CM seen in our environment were largely within the 2nd trimester accounting for 90 % of the gestational ages with majority showing degenerative changes like calcifications
Conclusion: In conclusion, the pattern of staining of CM amongst African origin has been found to be comparable with that of developed countries despite the commoner mid trimester presentation and degenerative changes

OFP-06-002
Novel markers for distinguishing gonadal elements in disorders of sex development with gonadal dysgenesis
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Objective: To propose a panel of immunohistochemical markers that can contribute to distinguish male, female and steroid-producing gonadal elements in disorders of sex development (DSD).
Method: FOXL2 is required for granulosa cell differentiation and expressed in ovarian stroma. Its counteracting transcription factor SOX9 is a target of SRY and essential for testis development by formation and maintenance of Sertoli cells. DMRT1 represses FOXL2 and is necessary to maintain testis differentiation. CYP11A1 and StAR are enzymes in the testosterone biosynthetic pathway. This panel was applied to 15 cases of dysgenetic gonadal tissue in 10 patients with DSDs.
Results: In ovo-testis and mixed gonadal dysgenesis, the sex cord-stromal cells of ovarian type tissue (Granulosa cell lineage) expressed FOXL2. Streak gonads showed a similar expression pattern of FOXL2 as normal ovarian-type stroma. Sex cord-stromal cells in testicular type tissue (Sertoli cell lineage) showed nuclear staining of SOX9 and DMRT1, including Sertoli-cell hamartoma. CYP11A1 and StAR highlighted the presence of steroid-producing cells.
Conclusion: Based on the distinct expression of FOXL2, SOX9 and DMRT1 in dysgenetic gonads, our findings support that this panel is useful to distinguish male and female gonadal components. CYP11A1 and StAR are useful for identification of steroid-producing cells.

OFP-06-003
Two cases of bilateral hyperplastic perilobar nephroblastomatosis mimicking Wilms tumour: A case study with serious clinical impacts
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Objective: Nephrogenic rests (NRs) are the precursors of Wilms Tumour (WT) and have different stages in their life-cycle. Most NRs are microscopic, but hyperplastic NRs can grow expansively and mimic WT.
Method: Two children with lesions in their kidneys. Patient 1: A 9 month old male with bilateral, 1–6 cm, encapsulated, partially necrotic nodules, mainly of epithelial structures. Patient 2: A 23 month old female with multiple, 1–4 cm, partly encapsulated nodules of mainly epithelial structures, with some regressive changes.
Results: Despite the encapsulation, size and chemotherapy-induced changes (CIC) of these nodes, the diagnosis of bilateral hyperplastic nephroblastomatosis was made.
Conclusion: NRs are more common than we might think and hyperplastic NRs can mimic WT. Literature data are quite scarce on this topic and based on USA material, where preoperative chemotherapy is not used, thus lack the experience of chemotherapy effects on NRs. According to these papers, the best discriminative feature of WTs is encapsulation, which in fact can occur in NRs due to preoperative chemotherapy (usually given in Europe). Based on literature, one can over-diagnose hyperplastic NRs as WT and give wrong treatment. There is a need for update in literature data on hyperplastic NRs and their appearances after chemotherapy.

OFP-06-004
Sarcoma with CIC-DUX4 gene fusion: Case report of kidney tumour location in a 12-year-old boy
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Objective: Recent molecular advances have identified a novel sarcoma defined molecularly by oncogenic fusion of the genes CIC and DUX4 termed CIC-DUX4 sarcomas. The most common site of involvement was the trunk but some cases have been described in the head and neck and extremities. We report one of the first cases of primitive renal CIC-DUX4 sarcoma

Method: A 12-year-old boy who presented a renal tumour, a vena cava thrombus and lung metastases. CT scan confirmed the tumour size (70 x 78 x 72 mm), revealed a rupture of the renal capsule and an infiltration of the peri-renal fat and psoas.
Results: The morphological and immunohistochemical analysis showed an undifferentiated sarcoma. Molecular analysis demonstrated a CIC-DUX4 translocation, confirmed by FISH. Despite treatment with chemotherapy, the evolution was unfavorable and the patient died 17 month after the diagnosis in a context of brain metastases.
Conclusion: The diagnosis of sarcoma with CIC-DUX4 gene fusion is difficult in lack of specific pathological characteristics emphasizing the need for molecular analysis. Treatment has not yet been codified for these very aggressive tumours.

OFP-06-005
Congenital isolated cardiac anomalies: A retrospective study
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Objective: Congenital cardiac anomalies are the most common birth defects, with a prevalence of 76.11 per 10,000 births and 24,402 cases detected in Europe between 2010 and 2014. The aim of this study was to evaluate the incidence, spectrum and genetics of isolated cardiac anomalies, along with its correlation between prenatal diagnosis and fetal autopsies.
Method: Retrospective study of fetal autopsies performed between 2005 and 2016, in Centro Hospitalar e Universitário de Coimbra, with analysis of isolated cardiac anomalies, defined by excluding all with other major anomalies and those associated with chromosomal abnormalities.
Results: Among 223 fetal autopsies with cardiac anomalies, only 44 (19.7 %) matched the criteria, 40 of these with prenatal diagnosis. The median maternal age was 31 years and the median gestational age was 24 weeks. The three most common defects were complex anomalies, 17 cases (38.6 %); hypoplastic left heart, 10 cases (22.7 %) and ventricular septal defect, 7 cases (15.9 %). There was strong agreement between prenatal ultrasonography and autopsy findings (Kappa = 0.659, CI95% 0.506–0.812, $p < 0.005$). Genetics revealed one case of Apert syndrome and another of sarcoglycanopathy.
Conclusion: Isolated cardiac anomalies are a group of uncommon conditions with major impact, most without a genetic known cause, highlighting the importance of an accurate prenatal ultrasonography.

OFP-06-006
Mucinous adenocarcinoma in situ with K-RAS mutation in a newborn with antenatal diagnosis of congenital pulmonary airway malformation
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Objective: Congenital pulmonary airway malformation (CPAM) is characterized by multicystic lung mass. Type 1 CPAM are the most frequently and can be associated with mucinous adenocarcinoma in situ (MAIS). We report the first case of MAIS with KRAS mutation with antenatal diagnosis.
Method: A female neonate had a prenatal history of compressive macro cystic CPAM of the right lung detected during the third trimester. At birth, moderate signs of respiratory distress led to oxygen therapy. Fifteen days after birth a right lower lobe lobectomy was performed and cured the baby.
Results: At gross examination, the resected lobe harboured a multicystic area, with cysts wider than 2 cm. Histologically, this area showed a type I CPAM, with cysts lined by bronchial epithelium displayed on a smooth muscle layer. Numerous clusters of mucinous cells were found to line the adjacent alveolar walls, without invasive carcinoma component. Those extra-cystic mucinous cells expressed HNF4-α but were negative for TTF1. Molecular studies detected a KRAS gene mutation on exon 2, encompassing its precursor part in mucinous malignancies.
Conclusion: This case demonstrates that type I CPAM, should be considered as preneoplastic lesions, be completely resected in the first weeks of life and be tested for KRAS gene mutation.

OFP-06-007
Complex congenital heart anomalies: Correlation and agreement between prenatal diagnosis and routine autopsies
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Objective: The purpose of this study was to evaluate the correlation between prenatal diagnosis (PD) and fetal autopsy with congenital heart anomalies from 2006 to 2016.
Method: A retrospective study of fetal autopsies at Centro Hospitalar e Universitário de Coimbra, Portugal was performed and analyzed all cases with complex cardiac anomalies. In the cases with PD, a correlation between prenatal and post-mortem findings was made.
Results: A total of 1,372 fetal autopsies were performed. Cardiac anomalies were found in 226 cases, from which 46 (20.3 %) had complex congenital anomalies. We excluded 7 cases due to lack of PD. From the remaining 39 cases, median maternal age was 32-years-old and the median gestational age was 25 weeks. There was total agreement in 27 (69.2 %) cases. Ten cases had only partial agreement and two cases is total disagreement. The more common heart anomaly found here left arterial isomerism, atrioventricular septal defect with aortic arch anomalies and double outlet right ventricle with valvular anomalies.
Conclusion: We found a good correlation between PD and port-mortem findings. Two cases had total disagreement, presenting with oligohydramnios that can justify the absence of cardiac alterations during prenatal ultrasonography. The remaining cases presented other cardiac findings plus the described in ultrasonography.

OFP-06-008
Bilateral meconium hydrocele: An uncommon case
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Objective: Meconium hydrocele is a rare benign reason of scrotal masses in newborns caused by meconium leakage due to in utero intestinal perforation. Meconium reach the scrotal sac via patent processus vaginalis. Herein, we present a rare reason of scrotal mass in a newborn and its histopathological features.
Method: A 4 days old male baby was brought to the hospital due to restlessness and reluctance feeding. Detailed physical examination revealed that scrotum was firm on palpation. Scrotal ultrasound demonstrated anechoic mass including milimetric calcifications, measuring 2,5 cm in diameter on the posterior side of both testicle. Excision of the masses was performed at the age of 1 month.
Results: Gross pathologic findings were, oval shaped lump with variable consistency from soft to firm and yellowish green cut surface, measuring 4 × 1.5 × 0.8 cm diameters on the right side and 2 × 1 × 1 cm diameters on the left side. Microscopic examination demonstrated fibromyxoid connective tissue containing mucin lakes, dystrophic calcifications, scattered hemosiderin-laden macrophages, bile pigment, lanugo hair and occasional squamous cells.
Conclusion: When a scrotal mass is present in infants and young children, this rare benign entity should be considered to decide on the choice of treatment modalities.

OFP-06-009

Undifferentiated (embryonal) sarcoma of the liver: An acute presentation

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Objective: The undifferentiated (embryonal) sarcoma of the liver (UESL) represents 9–15 % of the paediatric primary malignant tumours of the liver, being the third most common hepatic malignancy in this epidemiological group; the majority presents in children from 6 to 15 years old. We report one of a total of two UESL cases diagnosed in the southern Portuguese tertiary care institutions within 10 years, in a patient whose age was higher than anticipated.
Method: A 17 year-old female referred to the emergency room with severe abdominal pain; preliminary imaging studies revealed liver rupture and hemorrhage stemming from a 19 × 16 × 12 cm solid lesion with cystic areas in the right hepatic lobe. The patient underwent embolization of the right branch of the hepatic artery and, a few days later, partial hepatectomy.
Results: Multiple tumour fragments were received, the largest measuring approximately 7 cm in greatest dimension. Grossly, the cut surface was glistening, with hemorrhagic cystic areas. Histologically, a malignant spindle-cell tumour was observed with morphologic and immunohistochemical features that led to the diagnosis of UESL.
Conclusion: UESL is associated with poor prognosis only avertible by complete surgical resection and adjuvant chemotherapy. In our case the tumour relapsed leading to a fatal outcome 67 days after the surgery.

OFP-06-010

Persistent localised interstitial lung emphysema associated with CPAP therapy: A case report

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Objective: Pulmonary interstitial emphysema (PIE) is abnormal collection of gases inside the connective tissue of the peribronhovascular tissue, interlobular septa and visceral pleura. It is not an uncommon finding in premature infants who need respiratory support by mechanical ventilation. (Bhojani et al, 2008). Only few cases of spontaneous PIE in unventilated patients are described (Bawa et al; 2014)
Method: We presented an immature baby with persistent PIE on continuous positive airway pressure (CPAP) therapy.
Results: A 30 week gestation male infant from twin pregnancy was born in a vaginal delivery. He was placed on nasal CPAP which was stopped in 3rd day of life and renewed again in the 5th day of life. No PIE was found in X-ray investigation. In the 20th day of life symptoms of sepsis was developed and patient suddenly died. In the autopsy was found cystic lesion of the upper lobe of the left lung. Histological investigation showed appearance of interstitial cysts lined with multinucleated giant cells consistent with persistent PIE.
Conclusion: 1. Localized PIE can occur for children treated with CPAP therapy only. 2. Localized PIE can predispose patient to worse prognosis even without appearance of pneumothorax and pneumomediastinum.

OFP-06-011

Microcephaly beyond the Zika virus: A two-center study with discussion of etiopathogenesis

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Objective: Microcephaly doesn't have a consensual definition. Classically it has been defined as a head circumference more than 2 standard deviations (SD) below average. However, this criterion can't be used alone for diagnosis, as if it were, 2.3 % of the general population would be microcephalic. We aim to characterize this malformation in the context of fetal autopsies.
Method: We consulted 6 years of data from two centers. Cases with microcephaly were identified and analyzed according to: maternal and obstetric history, fetal pathology and etiopathogenesis.
Results: In 2565 autopsies, 31 cases (1.2 %) of microcephaly were identified. 29,1 % were considered severe (3 SD below average). M:F ratio was 3:5. Average gestational age was 25w + 3d. 38,7 % were medical interruptions and 35,5 % were intrauterine deaths. Median maternal age was 32 years; 12,9 % had history of previous abortion and more than 20 % had accompanying maternal pathology. Most cases were associated with chromosomal or genetic abnormalities and in two cases a history of maternal Zika virus infection (ZVI) was identified.
Conclusion: Recently, greater attention has been given to microcephaly associated with ZVI. However, microcephaly has variable etiologies, which our study highlights. Early echographic detection and a complete fetal autopsy are fundamental, enabling a proper etiological diagnosis and genetic counseling.

OFP-06-012

Rare case of bifid cardiac apex associated with incidental neuroblastoma described in a first trimester fetus using 7Tesla post mortem-MRI and conventional autopsy

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Objective: Bifid cardiac apex is an unusual congenital anomaly described in marine mammals and rarely encountered in humans, being reported in less than 10 cases worldwide. We describe a case of bifid cardiac apex, discovered at the post mortem examination of a 13 weeks fetus.
Method: The pregnancy resulted after the artificial insemination of a 36 years old patient, diagnosed with hereditary thrombophilia. The spontaneous abortion occurred at 13 weeks of gestatinon, after adequate tracking of the pregnancy. The fetus was analyzed postmortem, firstly imagistic using a 7 Tesla Magnetic Resonance Imaging scanner and after by stereomicroscopic conventional autopsy.
Results: Both postmortem examinations revealed the heart in situs solitus with a bifid apex having a notch of 0,82 mm. The four chambers and the great vessels origin presented normal aspect, but the aortic arch was narrowed in the preductal level. Microscopic examination of the organs also revealed a neuroblastoma arising in the left adrenal gland, with local invasion and metastasis in the contralateral kidney, mediastinum and placental villi. The umbilical cord had normal histology, without tumoural emboli in the examined sections.
Conclusion: We present the first case of bifid cardiac apex identified in a first trimester fetus.

Monday, 4 September 2017, 17:15–19:15, G109
OFP-07 Joint Session: Soft Tissue and Bone Pathology / Nephropathology

OFP-07-001

Immunohistochemical expression and prognostic significance of PD-L1 and PD-1 in Ewing sarcoma family of tumours (ESFT)

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Objective: Ewing sarcoma family of tumours (ESFT) are aggressive neoplasms with scant tumour-infiltrating lymphocytes. We analyzed the

immunohistochemical (IHC) expression of PD-L1 and PD-1 and their prognostic significance in clinically localized neoplasms in a cohort of 370 ESFT.
Method: Slides prepared from tissue microarrays were stained for PD-L1 and PD-1 (Thermo Fisher Scientific, Dako Envision K8000). Membranous/cytoplasmic staining over 5 % of tumour cells was regarded as positive.
Results: PD-L1 expression was present in 19 % of ESFT, while PD-1 was expressed in 26 %. Forty-eight percent of tumours were negative and 12 % were positive for both PD-L1 and PD-1. Metastatic tumours displayed higher expression of PD-L1 ($p < 0.0001$). Histological subtypes were not correlated with PD-L1 or PD-1 positivity. ESFT with elevated proliferation index (Ki-67) were associated with higher PD-L1 expression ($p = 0.049$). Regarding prognosis, no significant association was found between PD-L1 expression and progression free survival (PFS) or overall survival (OS), whereas lack of PD-1 expression in tumour cells was correlated with both poor PFS ($p = 0.02$) and poor OS ($p = 0.004$)
Conclusion: PD-L1 expression was not significantly related to prognosis. PD-1 was expressed in 26 % of ESFT tumour cells and may have prognostic and therapeutic implications. Supported grant No.18814 EuroBoNeT and IVO Foundation.

OFP-07-002
Superficial CD 34-positive fibroblastic tumour: A morphological and immunohistochemical report of two cases
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Objective: Superficial CD 34-positive fibroblastic tumour (SCPFT) is a recently proposed term by Carter et al of a mesenchymal tumour of borderline malignancy with distinct morphological and immunohistochemical feature. The morphology of the spindle cells is that of marked pleomorphism with polygonal cells, prominent nucleoli, granular cytoplasm, xanthomatous areas and nuclear pseudoinclusions. Two cases previously diagnosed as atypical fibrous histiocytoma and dermatofibrosarcoma protuberance were reevaluated, both were females aged 28 and 38 years respectively presenting with a mass measuring 1.0–2.5 cm on the right wrist. The two lesions were subjected to five immunohistochemical stains.
Method: Five antibodies were used based on Genemed biotechnology protocol. The antibodies include CD34, CD68, Ki 67, AE1/AE3 and Desmin.
Results: The morphology is that of circumscribe dermal lesion with admixture of spindle and polygonal cells having prominent nucleoli and granular cytoplasm. Some areas show xanthoma cells. Few nuclear pseudoinclusions are seen. Immunoreactivity in both lesions was diffusely positive for CD34 and focal positive areas for AE1/AE3 stain. Ki 67 was less than 5 %. Xanthoma cells were positive for CD68. Desmin was negative.
Conclusion: SCPT is a new entity in the family of cutenous CD34-positive spindle cell tumours. It is important to differentiate it from malignant fibrous histiocytoma, atypical fibrous histiocytoma, dermatofibrosarcoma protuberans, malignant granular cell tumour and many other pleomorphic soft tissue tumours to prevent unnecessary treatment to the patient.

OFP-07-003
Low-grade fibromyxoide sarcoma: A review of cases from 2000 to 2017 in La Paz University Hospital
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Objective: Low-grade fibro-myxoid sarcoma (LGFMS) is an unfrequent low grade sarcoma. We reviewed all the cases diagnosed as LGFMS in our center during the last 17 years.
Method: We reviewed 13 cases diagnosed as LGFMS in Hospital La Paz, Madrid in the period 2000–2017. Clinical data and histopathological features were analyzed.
Results: 7 patients were men and 6 women with a mean age of 42.3 years. The most common locations were the thigh and the gluteus. Twelve cases presented in deep localisations. All patients went under surgery and 7 cases received adjuvant therapy. The tumour was a single mass on 12 cases with a mean size of 9.5 cm. All cases showed the typical histomorphology and 2 cases had giant rosettes with collagenized centers. Ten cases were positive for MUC4. Two cases were reclassified. Local recurrence was observed in 1 patient and 2 cases presented with pulmonary nodules.
Conclusion: LGFMS should be suspected when a mass appears as a benign fibrous and myxoid tumour with low proliferation. The giant-rosette variant is rare and non-specific. MUC4 is a specific tool in these cases (90.9 % in the studied cases).The low rate of local recurrences and metastasis in our study is probably due to the short follow-up.

OFP-07-004
Morphological changes in denosumab-treated giant cell tumour of bone: A diagnostic challenge
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Objective: To analyze clinical data and histological changes in 10 cases of giant cell tumour of bone (GCTB) treated with denosumab and surgically removed.
Method: 7 women and 3 men, median age of 31 (range 16–43) years. Denosumab treatment: 7 to 20 (median 11) months. Tumour location: femur (3), humerus (2), and tarsal scaphoid, iliac, radius, tibia and metacarpus (one each). Tumour size: 2 to 11 (median 5) cm. Treatment indications: inoperability (5); relapse (4) and persistence after curettage (1).
Results: Post-denosumab histological findings included: complete absence of giant cells (GC) in 9/10; residual foci of GC (1/10); neoossification (10/10), inflammation with lymphocytes and foamy histiocytes (9/10); secondary aneurysmal bone cyst (1/10). Two cases showed pseudosarcomatous changes consisting of fusiform growth pattern with mild to moderate cytological atypia, atypical chondroid differentiation and bone pseudoinfiltration. All cases were free of relapse with a follow-up of 16 (range 1 to 81) months.
Conclusion: Our series confirms the efficacy of denosumab therapy for managing inoperable or recurrent GCTB. It induces different histological changes, some of which could suggest a malignant transformation (osteosarcoma or malignant GCTB). The knowledge of this treatment is essential in order to avoid a misdiagnosis of malignancy.

OFP-07-005
GNAS mutation in low-grade deeply located myxoid soft tissue tumours
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Objective: Non-distinctive low cellularity makes differential diagnosis of deep low-grade myxoid soft tissue tumours challenging on biopsy, and surgical management actually differs among these entities. Mutations of GNAS gene are reported in up to 61 % of cases of intramuscular myxoma (IM). We aimed at assessing if Next Generation Sequencing (NGS) of GNAS can aid in differential diagnosis.
Method: Consecutive cases of deep low-grade myxoid soft tissue tumours that underwent NGS (Iontorrent-Hot-Spot-Cancer Panel) for GNAS from May 2016 to April 2017 were retrieved. Clinical, pathological and molecular data were extracted.
Results: Fifteen patients met the selection criteria. Most of them were females ($N = 11$), with a median age of 60 years. The most common site

was the thigh ($N = 8$). Mean size was 4.6 cm (interquartile range 3–6 cm). Tumours were seated "intramuscular" ($N = 13$) or "within muscular fascia" ($N = 2$). NGS analysis was evaluable in 14 patients. Several gene mutations, producing a constitutively activated protein R201Y, were identified in 11 cases, that were consequently diagnosed as IM. Three cases did not harbour GNAS mutations: two myxofibrosarcoma, low-grade, and one IM.
Conclusion: NGS for GNAS can be helpful in differential diagnosis of deep low-grade myxoid soft tissue tumours. Prevalence of GNAS mutation in this series was higher than expected requiring confirmation in a larger study.

OFP-07-006
Metastatic patterns of soft-tissue sarcomas: A single-institution series of 167 patients
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Objective: Detailed data on metastatic patterns of soft-tissue sarcomas (STS) is limited. We aimed to evaluate these patterns and factors influencing survival.
Method: All cases ($n = 167$) of recurrent STS were retrieved from our files (2010–2016). Clinicopathological data was analyzed. Statistical analysis was performed.
Results: First recurrence occurred only at the primary site in 64 patients, at distant location in 92 and both locally and at distance in 11. The most common locations were the primary site ($n = 75$), lung ($n = 54$) and lymph nodes ($n = 27$). Seventy-two patients had a second relapse, mostly locally ($n = 33$), lung ($n = 12$) and soft tissue ($n = 10$). Thirty patients had three or more relapses. Our series included 26 histological types, the most frequent being leiomyosarcoma ($n = 35$) and dedifferentiated liposarcoma (DDL) ($n = 24$). At first recurrence, the most common metastatic location was lung for leiomyosarcoma and the primary site for DDL. Survival after recurrence was lower for patients with distant metastases at first recurrence (HR = 3.63 [2,19-6,04]).
Conclusion: To the best of our knowledge this is one of the few studies regarding metastatic patterns encompassing various STS subtypes. Although lung was the most common distant site, other locations were also frequent. Site of first recurrence was influenced by histological type and it was a prognostic indicator.

OFP-07-007
The impact of acute kidney injury of donor kidneys transplanted with a low Remuzzi score on incidence of delayed graft function and long term outcome
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Objective: Kidney transplantation from acute kidney injury (AKI) donors has become more common. Most of the clinical diagnoses of AKI are treatable entities difficult to recognize without biopsy. We investigated the potential associations between clinical-defined deceased donors with severe AKI, pre-implantation histological findings and recipient outcomes
Method: Remuzzi score and acute tubular necrosis were assessed on kidney biopsies from donors classified using the AKI network (AKIN) criteria. Differences in incidence rates of delayed graft function (DGF) and short/long-term rejection between recipients transplanted with normal, AKIN 1, 2 and 3 donors were evaluated
Results: Sixteen out of 335 donors had AKIN 3 with a median serum creatinine of 458 umol/l. Fourteen (88 %) had a low (0–3) Remuzzi score and were used for single kidney transplantation and two (12 %) were used for dual kidney transplantation (Remuzzi score: 4–6). The rate of recipients from AKIN 3 donors with DGF (47 %) differed significantly by that in the other groups ($p = 0.013$) while the rate of cumulative rejection (45,5 %) at 24 months was not significantly increased
Conclusion: Recipients receiving AKIN 3 kidneys, selected with Remuzzi histopathological score, had a greater incidence of DGF but a similar long-term mean graft failure compared to other donors

OFP-07-008
Structural and functional analysis of human podocytes (morphometry of foot processes) under podocytopathies
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Objective: The aim of this investigation was to study ultrastructural characteristics of the foot process effacement and denudation the glomerular basement membrane, as an expression of podocyte dysfunction.
Method: Next podocytopathies were analyzed: focal segmental glomerulosclerosis (FSGS-8), membranous nephropathy (MN-17), minimal change disease (MCD-12). Nephrobiopsies were investigated by the light and electron microscopy . Morphometry of foot process effacement (FPE) of podocytes and % "denudation" glomerular basement membrane (%DGBM) were completed. Standard laboratory tests were performed.
Results: In various podocytopathies observed significant changes in the ultrastructure of podocytes caused the disorders of the selective permeability the glomerular filter. These changes were characterized by dysfunctional foot process effacement and "denudation" of glomerular basement membrane.Expressed atrophy of the parenchyma as glomerulosclerosis (GS) of all patients had a negative correlation with the GFR (glomerular filtration rate)- the main indicator the preservation of renal function. Correlation analysis FPE values and %DGBM revealed a statistically significant negative relationship.
Conclusion: We suppose that changing the podocytes is preventively—adaptive response of cells to the possibility of exfoliation from the surface of the GBM under stress and the action of damaging factors.

OFP-07-009
Development of a new renal pathology coding list for the Flemish Regional Biopsy Registry
A. Dendooven*, W. Laurens, M. Helbert, P. de Paepe, A. S. de Vriese, E. Lerut, T. Q. Nguyen
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Objective: Disease classification systems are increasingly used to encode clinical findings and to document the incidence of disease. As such, the (SNOMED-CT based) ERA-EDTA classification is used in Belgium for registering diagnosis in dialysis patients. However, the ERA-EDTA classification is a clinical, not a pathological system.
Method: The Flemish Collaborative Glomerulonephritis Group (FCGG), a joint effort by pathologists and nephrologists, is setting up a renal biopsy registry. To this end, we designed an up-to-date renal pathology coding list, to be used in addition to clinically based coding systems.
Results: The FCGG coding system consists of 60 possibilities, organized according to prevailing concepts: (1) proliferative glomerulonephritides, (2) podocytopathies/entities associated with nephrotic syndrome (3) monoclonal gammopathy-associated, (4) vascular, and (5) tubulointerstitial diseases, (6) rare entities and uncertain diagnoses. Link: http://www.nbvn.be/sites/default/files/uploads/fcgg-nbvn_pa_coderingslijst_voor_nefropathologische_codering-1.pdf All renal pathologists in Flandres are now using the coding system in a structured report. Peer review meetings will promote diagnostic consistency.

The Flemish Renal Biopsy Registry contains clinical and pathological data including FCGG code from all non-transplant biopsies, starting from Jan 1st 2017.
Conclusion: We have designed a renal pathology coding system along with setting up the Flemish Renal Biopsy Registry. Future efforts will be made to validate the FCGG system for renal biopsy registration.

OFP-07-010
How successful is an experienced nephropathologist in diagnosing adult minimal change disease when electron microscopy is not accessible?
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Objective: Minimal change nephrotic syndrome is considered as a diagnosis of electron microscopy (EM). However, EM facility is not available in every institution. In this study, we aimed to explore the success rate of minimal change disease (MCD) diagnosis in the renal biopsies of adult nephrotic patients in which EM was not performed.
Method: 79 adults which were given possible diagnosis of MCD by one of 2 experienced nephropathologists between 2000 and 2016 in a single institution were investigated for their therapy response. Biopsies had been studied by light and immunofluorescence microscopy without EM. Only the patients who had ≥6 months follow-up after immunosuppressive-therapy were included ($n = 43$).
Results: All patients responded to treatment. 38 showed complete whereas remaining 5 had partial remission. None of the patients progressed to chronic renal disease. There were no histological differences between cases showing partial or complete remission. Ratio of globally sclerosed glomeruli ranged between 0 and 30 %. IF/TA involved ≤25 % of cortex. Interstitial inflammation and vascular sclerosis were mild if present.
Conclusion: Response rate to immunosupressive-treatment in our MCD patients were similar to other series. This may indicate that diagnosis of MCD can be suggested reliably by experienced nephropathologists without contribution from EM which may not be accessible due to various reasons.

OFP-07-011
Clinicopathological correlation of findings in patients with renal and bone marrow biopsies
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Objective: Monoclonal gammopathies (MG) can cause renal impairment and proteinuria. Amyloidosis, cast nephropathy, light chain deposition disease (LCDD) and glomerulonephritis can be seen in renal biopsies secondary to hematological diseases. We aimed to examine the clinicopathological findings of the patients having both bone marrow and renal biopsies.
Method: Between 2012 and 2015, 1030 patients had obtained renal biopsy in our center. One hundred thirty of them had also bone marrow biopsy(12.6 %). We reevaluated the bone marrow and renal biopsies of all cases in the aspect of clinical and laboratuary findings.
Results: Among 130 cases that had both bone marrow and renal biopsy 40 were diagnosed as multiple myeloma and plasma cell dyscrasia in bone marrow biopsies. Among these cases, the most common findings in renal biopsies were AL amyloidosis (57.5 %); cast nephropaty (25 %); tubular injury (10 %); tubular interstitial nephritis (TIN) (0,2 %); LCDD (0,2 %). Forty-nine cases were diagnosed as renal amyloidosis (37.7 %). In bone marrow biopsies of 15 cases that had renal amyloidosis, amyloid deposition was not identified. Among the renal amyloidosis patients, 23 were evaluated as AL, 12 were AA; 4 were nonAA/AL, one case was ATTR; 9 cases couldn't be subtyped. AL amyloidosis was the most common renal morphological finding in our study. We found lower rates of tubulopathy and LCDD when compared to literature.
Conclusion: Clinicopathological correlation and awareness of renal manifestations associated with MG are important in the evaluation of renal biopsies. Data about glomerular pathological findings associated with monoclonal gammopathies is limited and need further investigations.

OFP-07-012
NCAM and FGFR1 over-expressions are the earliest molecular changes upon TGF-β induced renal fibrosis in vitro—key targets for further strategies to ameliorate renal fibrosis
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Objective: The major challenges are to look deeper into signaling pathways driving renal fibrosis and to define key molecular changes underling such process.
Method: TGF-β-induced epithelial-mesenchymal transition (EMT) of kidney tubular epithelial cells (HK-2 cell line) was used as an established in vitro model of renal fibrosis. HK-2 cells were seeded in 6-well plate divided in control, TGF-β treated and TGF-β + FGFR inhibitor (PD173074) treated groups. EMT changes were followed optico-microscopically, using immunolabeling and qRT-PCR, following dynamical changes of gene expression.
Results: TGF-β induced EMT was morphologically clearly visible after 72 h. However, molecular changes characteristic for EMT were detected earlier: 48 h after TGF-β treatment relative mRNA levels of SLUG, SNAIL, TWIST, MMP2, MMP9, N-cadherin, integrin-α5, α-SMA and FSP-1 were significantly up-regulated and E-cadherin was down-regulated in TGF-β group ($p < 0.001$). Even more, NCAM and FGFR1 molecules achieved their pick of over-expression 24 h after EMT induction. These changes revealed completely new approach to our further experiments and lead us to try to inhibit EMT events by administration of PD173074. Surprisingly, PD173074 restores all EMT induced changes including morphology and molecular characteristics.
Conclusion: NCAM and FGFR1 were the earliest over-expressed gens upon TGF-β induced EMT of HK-2 cells and PD173074 almost completely prevented TGF-β induced EMT, suggesting potential of PD173074 to ameliorate renal fibrosis.

Tuesday, 5 September 2017, 08:30–12:00, G109
OFP-08 Breast Pathology

OFP-08-001
Prognostic significance of tumour-infiltrating lymphocytes according to molecular subtype in breast cancer patients who received adjuvant chemotherapy
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Objective: This study investigated prognostic value of tumour-infiltrating lymphocytes (TILs) according to molecular subtype of invasive breast cancer (IBC) in patients who received adjuvant chemotherapy.
Method: TILs were evaluated in 1,269 IBCs using the standard method and the cases were classified into high and low TILs groups based on a 10 % cutoff. Correlations of TILs with clinicopathological characteristics and prognosis were investigated.
Results: Of the 1,269 IBC patients, 388 (30.6 %) had high TILs and 881 (69.4 %) had low TILs. High TILs was associated with ER and PR

negativity ($P < 0.001$), HER2 positivity ($P < 0.001$), high histological grade ($P < 0.001$), large tumour size ($P = 0.028$), negative lymph node status ($P = 0.013$), absence of lymphovascular invasion ($P = 0.012$), and high Ki-67 ($P < 0.001$). Patients with high TILs had significantly longer overall survival (OS, $P = 0.011$) and disease-free survival (DFS, $P < 0.001$) than those with low TILs. In subgroup analysis, significant differences of OS and DFS according to TILs level were observed in luminal B, HER2-positive, and triple-negative subtypes. In multivariate analysis, high TILs was an independent factor for good prognosis (OS, $P < 0.001$ and DFS, $P < 0.001$).
Conclusion: TILs could be a useful prognostic and predictive marker of adjuvant chemotherapy in patients with IBC.

OFP-08-002
The relationship between Cyclin D1 expression and clinicopathologic prognostic parameters in invasive breast carcinoma
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Objective: In this study, we aimed to evaluate Cyclin D1 expression in patients with invasive breast carcinoma and underline its clinical and pathologic significance.
Method: The slides (both H&E and IHC) of patients ($n = 143$) who were diagnosed as invasive breast carcinoma in both partial and total mastectomy specimens between 2007 and 2013 in our department were reevaluated. Immunhistochemical analysis of Cyclin D1 [score = intensity (0-absent, 1-mild, 2-moderate, 3-intense) x percentage (1- <10 % , 2- 10-50 % , 3- >50 %)] and the classification with the final score (1-lack of expression, 2-weak, 3- strong) were done. The statitistical analysis (Pearson Chi-Square and Spearman's rho) was performed to reveal its relation to clinical and histopathologic parameters in breast carcinoma.
Results: No relation was found between patient age, T stage, tumour multifocality, lymph node metastasis or Modified Bloom Richardson(MBR) score and Cyclin D1 status. However, statistically significant ($P < 0.001$) and moderate positive($r = .32$) correlation was found between ER(Estrogen) and Cyclin D1 score. PR(Progesteron) and Cyclin D1 score correlation [($P < 0.001$) and $r = .31$)] was in the same level. In evaluation of different molecular subgroups of breast cancer, our cases in 'Luminal B' group significantly ($P = 0.008$) expressed more Cyclin D1 (%92.9 of 'Luminal B' were positive). 'Triple (-)' group significantly ($P = 0.008$) expressed less Cyclin D1 (%40 of 'Triple (-)' were negative).
Conclusion: The higher amounts of Cyclin D1 expression in Luminal B and Luminal A molecular groups and the positive correlation of Cyclin D1 and ER suggests that Cyclin D1 may play an important role in the pathway of estrogen-sensitive breast cancer.

OFP-08-003
Immunohistochemical analysis of the expression of breast markers in basal-like breast carcinomas defined as triple negative cancers expressing keratin 5
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Objective: Estrogen and progesterone receptors are possible markers for suggesting a mammary origin of metastatic carcinoma, but are useless in cases of triple negative breast cancers (TNBC).
Method: Five other potential markers of breast origin were investigated on tissue microarrays in a series of TNBCs showing keratin 5 expression, consistent with a basal-like phenotype.
Results: Of 115 TNBC cases any GATA-3, mammaglobin, GCDFP-15, NY-BR-1 and BCA225 immunostaining was observed in 82 (71.3 %), 30 (26.0 %), 23 (20.0 %), 7 (6.0 %) and 74 (64.3 %), respectively; using a >5 % staining cut-off, this dropped to 23, 12, 9, 3 and 40 cases, respectively. BCA225 is reported to stain many other malignancies, therefore lacks specificity. Coexpression of 3 and 2 markers was seen in 1 and 4 cases, respectively. Using 5 % staining as cut-off, the expression of any of 4 markers (excluding BCA225) was 34.7 %.
Conclusion: The expression of GATA-3, mammaglobin, GCDFP-15 and NY-BR-1 is lower in TNBC-s than in breast carcinomas in general, and this may be even lower in basal-like carcinomas. Although these markers are not fully specific, by using them, a subset of basal-like TNBC-s can be identified as of mammary origin. However, a substantial proportion will not stain with any of these markers.

OFP-08-004
Features of atypical ductal hyperplasia in high and low risk patients that predict upgrade to carcinoma
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Objective: A core needle biopsy (CNB) diagnosis of atypical ductal hyperplasia (ADH) is currently managed with surgical excision (SE) to exclude carcinoma (ca). We aim to identify features of ADH on CNB that predict upgrade to invasive ca or DCIS on SE.
Method: Review of ADH CNB diagnosed between 2009 and 2011 was performed. Cases were divided into high and low-risk based on the presence of personal history (Hx) of breast ca, Hx of breast or ovarian ca in a 1st-degree relative and positive BRCA carrier status.
Results: 140 cases of ADH diagnosed on CNB were identified. 122 (87.1 %) cases had SE, 76 in high-risk patients and 46 in low-risk patients, with an upgrade rate of 55.3 and 43.5 %, respectively ($p = 0.206$). In high-risk patients, the predictive features are: CNB done under ultrasound guidance (9 cases with upgrade vs 1 cases without upgrade, $p = 0.014$), personal Hx of ipsilateral breast ca (19 cases vs 3 cases, $p = 0.0001$) and older age at diagnosis (58 years vs 52 years, $p = 0.018$). In low-risk patients, the larger radiological lesion size (34.69 mm vs 10 mm, $p = 0.006$) was the only significant predictor of upgrade.
Conclusion: In our cohort, ADH diagnosed on CNB carried a significant risk of upgrade on SE, regardless of the risk status of the patients. Several radiologic and clinical features were found to predict upgrade on SE, and may be used to develop a predictive model that could help stratifying the risk of ADH diagnosed on CNB.

OFP-08-005
CD9 expression is associated with poor prognosis in patients with invasive lobular carcinoma
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Objective: This study aimed to investigate the prognostic significance of CD9 expression in patients with invasive lobular carcinoma (ILC).
Method: CD9 expression in tumour cells was evaluated by immunohistochemical staining (IHC) in 113 ILC samples. Correlations of CD9 expression with clinicopathological parameters and patient survival were assessed.
Results: Positive CD9 expression was observed in 48 (42.5 %) of 113 cases. CD9 expression was significantly associated with low level of tumour-infiltrating lymphocytes ($P = 0.042$) and classic subtype ($P = 0.038$). No significant correlation was found between CD9 expression and clinicopathological parameters including tumour size, lymph node status, lymphovascular invasion, hormone receptors, HER2 status, and Ki-67 labeling index. Patients with positive CD9 expression showed worse overall survival (OS, $P = 0.05$) and disease-free survival (DFS, $P = 0.014$) than those with negative CD9 expression. In multivariate

analysis, CD9 expression was an independent prognostic factor for DFS ($P = 0.049$).
Conclusion: CD9 could be a useful prognostic marker in patients with ILC.

OFP-08-006
Ex-vivo assessment of drug response on breast cancer primary tissue with preserved microenvironments
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Objective: Interaction between cancerous, non-transformed cells, and non-cellular components within the tumour microenvironment plays a key role in response to treatment. However, short term culture or xeno-transplantation of cancer specimens result in dramatic modifications of the tumour microenvironment, thus preventing reliable assessment of compounds or biologicals of potential therapeutic relevance.
Method: We used a perfusion-based bioreactor to successfully maintain the tumour microenvironment of freshly excised breast cancer tissue obtained from 28 breast cancer patients and used this platform to test the therapeutic effect of antiestrogens as well as checkpoint-inhibitors on the cancer cells.
Results: Viability and functions of tumour and immune cells could be maintained for over 2 weeks in perfused bioreactors. Next generation sequencing and analysis of phosphorylation status of selected proteins authenticated cultured tissue specimens as closely matching the original clinical samples. Anti-Programmed-Death-Ligand (PD-L)-1 and anti-Cytotoxic-T-Lymphocyte-Associated-Protein (CTLA)-4 antibodies lead to immune activation, evidenced by increased lymphocyte proliferation accompanied by a massive cancer cell death in ex vivo triple negative breast cancer specimens.
Conclusion: In the era of personalized medicine, the ex vivo culture of breast cancer tissue represents a promising approach for the pre-clinical evaluation of immune-mediated treatments and provides a platform for testing of innovative treatments.

OFP-08-007
Role of trefoil factor 3 in breast carcinoma chemoresistance
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Objective: Breast carcinoma is commonest cancer among UAE population and the most common cancer among females. Examination of the 5′ promoter regions of trefoil factor 3 (TFF3) gene has identified putative estrogen and progesterone receptor–DNA binding domains as direct response elements to estrogen and progesterone that are linked to breast functions or steroid regulation. The study was designed to determine the role of TTF3 in breast cancer chemoresistance with the aim of establishing TTF3 expression as a biomarker for drug resistance
Method: In total, 133 cases of breast carcinoma treated with neo-adjuvant therapy were collected. Tissue samples from pre-neo-adjuvant therapy as well as tissues from post-neo-adjuvant therapy of those cases were collected and stained with immunohistochemistry for TTF3,Bcl2, BAX, cleaved caspase-3, AKT-1 and NF kappa B.
Results: There was a significant correlation between the expression of TTF3 in breast carcinoma cells and response to neoadjuvant chemotherapy ($p = 0.0107$). There was significant co-expression of TTF3 with AKT1 ($p = 0.0336$), Bcl2 ($p = 0.0142$), and NFKB ($p = 0.0461$) in breast carcinoma cases with residual carcinoma following neoadjuvant therapy which support the role of TTF3 in chemoresistance.
Conclusion: There is a significant correlation between the expression of TTF3 by breast carcinoma cells and resistance to chemotherapy.

OFP-08-008
Evaluation of residual breast cancer for HER2 status with a combined gene-protein assay after neoadjuvant trastuzumab-based chemotherapy
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Objective: HER2-positive breast cancer (BC) patients who did not achieve pathological complete response (pCR) after neoadjuvant trastuzumab-based chemotherapy were investigated for phenotypic and genotypic HER2 status of residual tumour cells.
Method: 25 originally HER2-positive cases not achieving pCR were analyzed with HER2 gene-protein assay (GPA) for concurrent detection of HER2 gene and protein at individual cell level. Pre-treatment versus post-treatment HER2 status was determined with HER2 GPA on core needle biopsy and surgical resection samples.
Results: There was a mix of HER2 homogeneity and heterogeneity among cases before therapy. Overall HER2 gene amplified and protein positive tumour cells were significantly lowered among post-treatment residual tumours. However, there were two types of response in non-pCR cases: 1) little/no response (28 %) and 2) moderate/marked response (72 %). No HER2 protein positive cells were observed in 7 cases. In these cases persistent tumour cells were either negative for both amplification and protein overexpression or positive only for amplification.
Conclusion: Neoadjuvant HER2-targeted therapy effected reduction/elimination of HER2 protein-positive tumour cells even among non-pCR patients. Some patients may need a longer HER2 targeted-therapy for achieving pCR. It would appear however that loss of HER2 protein expression is a mechanism for breast cancer resistance to trastuzumab-based therapy.

OFP-08-009
HER2 intratumoural heterogeneity in breast cancer: Proposal of a new classification
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Objective: HER2 intratumoural heterogeneity (ITH) is evidenced in 5 to 40 % of breast cancer (BC) cases in published series. This wide range of proportions indicates a need for refining HER2 ITH classification.
Method: We analyzed a cohort of 124 HER2 positive BC cases, originally determined with both HER2 IHC and FISH, with HER2 gene-protein assay (GPA) for concurrent detection of HER2 gene and protein at individual cell level. Cases were classified as: 1) homogeneous (all HER2 gene-amplified & protein positive tumour cells); 2) HER2 genetic heterogeneity (GH: a mixture of HER2 gene-amplified & protein positive cells and HER2 gene non-amplified & protein negative cells); 3) HER2 micro-heterogeneity (MH: a mixture of HER2 gene-amplified & protein positive cells and HER2 gene-amplified & protein negative tumour cells); and 4) mixed GH + MH cases.
Results: Homogeneous cases represented 64 %, MH 29 %, GH 11 %, and GH + MH co-existed in 4 % of the cases. MH was far the most common type of HER2 ITH in this series.
Conclusion: Based on these GPA data, we propose a new classification of HER2 ITH that, in addition to HER2 GH, includes a new HER2 MH category.

OFP-08-010
Is regression after neoadjuvant chemotherapy for locally advanced breast cancer different in sentinel and non-sentinel nodes?
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Objective: Metastasis formation is not the only change known to occur in tumour-draining lymph nodes. Tumour-reactive lymphadenopathy is a complex reaction, which comprises morphological and functional changes that may alter the effect of neoadjuvant therapy in tumour-draining sentinel lymph nodes (SLN) compared to non-SLNs. Differences in the degree of regression induced by neoadjuvant therapy in SLNs and in non-SLNs were investigated.
Method: Neoadjuvantly-treated breast cancer patients who underwent SLN biopsy and axillary lymph node dissection were analyzed. All metastatic and non-metastatic SLNs and non-SLNs were evaluated and fibrotic foci in the lymph nodes were interpreted as signs of regression.
Results: Of the 142 cases, 89 showed signs of nodal regression. Greater regression in non-SLNs was found in 22 cases (22/89 cases, 25 %), whereas 18/89 cases (20 %) were in support of a more pronounced regression in the SLNs. The remaining cases demonstrated either an equal degree of regression in SLNs and non-SLN, or no regression.
Conclusion: Although the case numbers are relatively small there was no obvious difference in the degree of regressive histological changes shown by SLNs and NSLNs. Therefore, the effect of tumour-reactive lymphadenopathy may not be a major contributor to the somewhat higher false negative rate of SLN biopsy after neoadjuvant treatment.

OFP-08-011

Association between LAPTM4B gene copy number alterations and anthracycline based chemotherapy in hormone receptor negative breast carcinomas

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Objective: To determine the associations between LAPTM4B copy number alterations and response to different chemotherapy regimens in hormone receptor negative (HR-) primary breast carcinomas.
Method: Two cohorts were analyzed: (1) 61 core biopsies of HR- breast carcinomas treated with neoadjuvant chemotherapy (anthracycline-based in 72 % of patients and non anthracycline-based in 28 % of patients), (2) tissue microarray of 69 HR- tumours treated with adjuvant therapy (81 % of patients received anthracycline- and 19 % of patients non anthracycline-based therapy). Interphase FISH technique was applied using custom-made dual-labelled FISH probes (LAPTM4B/CEN8q, Abnova Corp.)
Results: Regarding neoadjuvant setting, in the anthracycline treated group significantly higher ($p = 0.037$) average LAPTM4B copy number was observed in the non-responder group (average LAPTM4B copy was 4.1) compared to pCR group (average LAPTM4B copy was 2.6). Regarding adjuvant cohort, in the anthracycline treated group the average gene copy number was higher in metastatic breast carcinomas compared to the non-metastatic ones ($p = 0.046$). In non-anthracycline treated group of patients we found no significant differences between responder vs. non-responder groups and between metastatic vs. non-metastatic groups.
Conclusion: Our results confirm the possible role of LAPTM4B gene in anthracycline resistance in HR- breast cancer. LAPTM4B copy number analysis may assist chemotherapy selection in the future.

OFP-08-012

Genes that enable cerebral metastasis of breast cancer

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Objective: Approximately 40 % of patients with systemic cancer will develop central nervous system (CNS) metastasis. The appearance of cerebral metastasis usually defines the terminal stage of disease for women suffering from disseminated breast cancer. Understanding the molecular basis of the tumour cells crossing the blood-brain barrier is crucial to prevent metastasis to the brain. Aim of the study: To identify new genes involved in the development of cerebral metastasis in breast cancer patients.
Method: The expressional profiles of primary breast cancer samples of patients with estrogen receptor negative (ER-) breast cancer with cerebral metastases were compared to the expression profiles of matched tumours of women with metastases to sites other than the brain. For profiling the Illumina WG-DASL RNA platform was used.
Results: The cell adhesion associated, oncogene regulated (BOC) and microtubule associated protein 2 (MAP2) were significantly highly expressed in breast cancer samples that metastasized to brain as compared to those samples that metastasized to other organs. The expression of these 2 genes were validated by RT-PCR and immunohistochemistry. Currently, we are carrying out functional studies to reveal the specific involvement of BOC and MAP2 in the formation of brain metastasis.
Conclusion: Boc and MAP2 are involved in the formation of cerebral metastases of ER—breast cancer. The molecular mechanisms need to be studied in order to develop preventional strategies.

OFP-08-013

T-lymphocytes induce the expression of GBP1 and facilitate brain metastasis of breast cancer

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Objective: In order to reach the brain tumour cells need to take the hurdle of the blood-brain barrier (BBB). Aim: To identify specific pathways involved in brain metastasis of breast cancer.
Method: We compared the gene expression profiles of estrogen receptor negative (ER-) primary breast cancer samples of women with metastasized disease, with and without brain involvement. Validations were done by IHC, RT-PCR and by using an in vitro BBB model. In addition, we discovered how T cells change breast cancer cells at the protein level by using liquid chromatography-mass spectrometer (LC-MS).
Results: We found genes related to "T cell response" to be prominently associated with the occurrence of brain metastasis. In functional studies using an in vitro BBB model, breast cancer cells that were co-cultured with T lymphocytes passed the artificial BBB with a 300–600 fold acceleration. Following, we identified 11 differentially expressed proteins in breast cancer cells that were co-cultured with T lymphocytes. After matching these proteins with gene expression profiles of the original patient datasets, we found that the gene for guanylate binding protein 1 (GBP1) was upregulated in the samples that were associated with cerebral metastasis. Silencing of GBP1 in breast cancer cells resulted in a 30–70 fold decrease of the passage of the breast cancer cells through the BBB model.
Conclusion: Expressional imprinting of breast cancer cells by T lymphocytes assists in the formation of brain metastases, which is a new insight in the complex interplay of T lymphocytes with cancer cells. This discovery is crucial to open opportunities for preventing the formation of brain metastases.

OFP-08-014

X-chromosome aneusomy and androgen receptor status in male breast cancer

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Objective: X chromosome gain has been previously described in male breast cancer (MBC). Androgen Receptor (AR) is located on X

Chromosome. A possible therapeutic role of AR in MBC is emerging in the recent literature. The aim of this study is to investigate the role of the X chromosome in MBC development.
Method: Seventy-three consecutive MBC cases were reviewed. When present areas of DCIS and gynecomastia surrounding the invasive carcinoma were also studied. Cases were tested by FISH to assess the X chromosome status and AR amplification, ICH for AR expression, and bisulfite-Sequencing for AR DNA methylation.
Results: X chromosome gain was observed in 74,7 % invasive MBC, in 20.6 % of DCIS and in 14.6 % of gyecomastia when associated to cancer. AR gene copy number increased parallel to the number of X chromosomes. On ICH, AR expression (positive staining in > 1 % of the neoplastic nuclei), was present in 96.6 % of invasive MBC tested. Absence of AR DNA methylation was detected for both epialleles in 9\cr10 cases.
Conclusion: These data confirm that X chromosome gain plays a role in the neoplastic transformation of male breast epithelial cells and is related with AR polysomy. AR gene copies appear to be unmethylated, therefore maintaining their function.

OFP-08-015
Axonogenesis and vascular proliferation are associated gene expression programs in hormone receptor negative breast cancer
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Objective: Interactions between cancer cells, vasculature and nerves have been suggested as important for tumour progress. We aimed to explore these relations in subtypes of breast cancer (BC), with particular attention to novel treatment targets.
Method: We analyzed multiple BC mRNA cohorts and signatures reflecting vascular proliferation and axonal sprouting were explored. A cohort of primary BC tissue ($n = 461$) was studied by IHC for validation (Factor VIII-Ki67; Neurofilament).
Results: High angio- and axonogenesis signature scores associated with ER/PR negativity, a basal-like phenotype and shorter survival. Notably, the angio- and axonogenesis scores were significantly associated, and a jointly activated neuro-angiogenic profile strongly associated with the basal-like phenotype and gene sets reflecting hypoxia and immune responses. An association between vascular proliferation and axon density by IHC was found. Through a drug signature database (Connectivity-Map), compounds with dopaminergic action were identified as negatively correlated with the expression profile of VP-high tumours.
Conclusion: Our findings indicate vascular proliferation and axonogenesis as coordinated programs in aggressive breast cancer. Dopaminergic drugs are suggested as potentially relevant, especially for the basal-like subtype with few treatment options.

Tuesday, 5 September 2017, 17:15–19:15, D203
OFP-09 Uropathology

OFP-09-001
Large nested variant of urothelial carcinoma in urinary bladder: Histopathological analysis in 18 transurethral resection cases
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Objective: Endophytic growth pattern in urothelial carcinomas (UC) cause problems in evaluation of invasion, especially in low-grade cases.
Method: Haematoxylin-eosin stained slides of bladder transurethral resection materials submitted to our department in 2008-2017 were re-examined. There were 18 UC cases with large nested pattern of invasion.
Results: The mean age was 70 and 83 % were male. Mean tumour diameter was 4,83 centimetres. Non-invasive UC component was present in all cases; low-grade in 6, high-grade in 1, low and high-grade in 11 cases. Twelve and 6 cases were pT1 and pT2, respectively. All cases had invasive component composing of medium-large nests. Additionally, 2 cases had focal small invasive nests and 2 cases had areas of conventional invasive UC. Stromal-tumour interface was irregular in 16 cases, whereas 2 cases had invasive nests with rounded contours. Fibrous stromal reaction and/or stromal lymphoid infiltration were present in 17 cases. "Budding", described as small nests in stromal interface of medium-large nests was a remarkable feature in 13 cases. Angiolymphatic invasion and necrosis were detected in 2 and 5 cases, respectively.
Conclusion: Large nested pattern of invasion in UC causes diagnostic difficulty. Irregularity of nests, presence of stromal reaction, "budding" and muscularis propria invasion can be helpful in differential diagnosis.

OFP-09-002
Descriptive statistical analysis of mismatch repair proteins (MLH1, MSH2, MSH6 and PMS2) immunohistochemical expression in prostate cancer: Correlation with Grade Groups (ISUP/WHO 2016)
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Objective: The role of DNA Mismatch Repair (MMR) genes in prostate cancer (PrCa) is poorly understood. We investigated the correlation between MMR protein expression (MLH1, MSH2, MSH6, PMS2) in PrCa and their relationship with Grade Groups (GG).
Method: Immunohistochemical expression of MMR proteins was assessed. GG and Nuclear Histoscore method (NH = 0-300) were used to group 126 PrCa cases (Parc Salut Mar-Biobank, Barcelona) in three categories: Group0, NH: 0–10; Group1, NH: >10–100; and Group2, NH: >100.
Results: In assessable TMA cores, MSH2 expression was lost in 7/108 (6.5 %), MSH6 in 54/97 (55.7 %), MLH1 in 11/114 (9.6 %) and PMS2 in 2/114 (1.8 %). The two last results were paradoxical compared to the general literature (lost MLH1/preserved PMS2, 7/114 cases, 6.1 %). MSH2/MSH6 heterodimer and MLH1/PMS2 losses were detected in 6/98 (6.1 %) and in 1/113 (0.9 %) cases, respectively. MSH6 loss was statistically associated with GG ($p = 0.005$), with most cases belonging to GG2.
Conclusion: This preliminary study supports the fact that MMR proteins role is poorly defined in PrCa. Unusual patterns are probably conditioned by tumour heterogeneity and intrinsic prostate tissue properties. These results must be correlated with molecular analysis in order to clarify their relationship with familial PrCa. Funding: Grants: ISC-III (PI15/00452), Jordi-Gras 2016.

OFP-09-003
Clinicopathologic analysis of Birt-Hogg-Dube Syndrome (BHD)-associated renal cell carcinomas (RCC)
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Objective: Birt-Hogg-Dube syndrome (BHD) is a newly emerging hereditary disorder caused by germline mutation of FLCN. Multiple renal cell carcinomas (RCCs) determine the prognoses of BHD patients. Most BHD-RCCs are chromophobe RCCs or hybrid oncocytic/chromophobe tumours (HOCTs). Differential diagnosis between BHD-RCCs and sporadic counterparts is important because FLCN mutation carriers have high risks of developing bilateral multiple RCCs. The aim of the study is to find useful markers for differentiation between BHD-RCCs and histology-matched sporadic counterparts.

Method: We investigated histopathologic characteristics of 67 surgically resected RCCs from BHD patients, using immunostaining, Western blotting, FISH/CISH, and DNA sequencing.
Results: Two histologic types, chromophobe RCC and HOCT, accounted for 82 % of BHD-RCCs. Normal-looking cortices often contained oncocytic/clear cell nests. BHD-RCCs showed overexpression of glycoprotein non-metastatic B (GPNMB) and underexpression of FLCN, whereas sporadic tumours showed inverted patterns. FISH/CISH analysis for the chromosomes 2p, 3p, 6p and 17q revealed disomic pattern in BHD-RCCs and frequent copy number losses in sporadic counterparts.
Conclusion: BHD-RCCs were often indistinguishable from sporadic RCCs in histology but had some characteristic molecular markers. Comprehensive analyses with the help of FISH/CISH and GPNMB immunostaining will help pathologists determine whether the cases should be considered for further genetic testing.

OFP-09-004
Impact of transperineal template biopsies on prostatic biopsy processing and analysis in Europe
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Objective: Prostatic transperineal template biopsies (TPTB) are performed for detailed cancer assessments after unexpected negative transrectal ultrasound biopsies (TRUSB) and for correlation with mpMRI findings. The impact of TPTBs has not been analysed.
Method: The European Network of Uro-Pathology distributed a survey on TPTB, including how specimens were received, processed and analysed.
Results: We received 244 replies from 22 countries with 167 respondents who received TPTB. Biopsies were received in more than 12 pots in 35.2 %. The number of cores per cassette varied between 1 (39.5 %) and 3 or more (39.5 %). 48.3 % cut three levels/block (range of 1 to >6 levels). The majority (79.4 %) reported Gleason score in each core or site and 59.6 % gave an overall score. The number of positive cores was always reported and 69.4 % gave details (measure, percentage, involvement and map). For 19.0 %, TPTB had adversely affected laboratory workload with only 27.0 % managing to negotiate extra costs.
Conclusion: Most laboratories process samples thoroughly and report TPTB similarly to TRUSB. TPTB have caused considerable extra work, which remains uncosted in most centres. Guidance is needed for workload impact and minimum standards of processing if TPTB work continues to increase.

OFP-09-005
Molecular subtyping of urothelial bladder carcinoma in young patients
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Objective: Recently, five major molecular subtypes of urothelial carcinoma have been determined: urobasal A, urobasal B, squamous cell cancer-like (SCCL), genomically unstable (GU), and a heterogeneous infiltrated class of tumours. Each of them is associated with distinct behavior and outcomes. It is suggested that urothelial carcinoma in young patients exhibits unique clinicopathological features.
Method: In our study, we applied the molecular classification to the cohort of urothelial carcinoma in patients younger than 45 years using a set of immuhistochemical protein expression patterns (CK5/6, CK20, CK14, CD44, p53, ERBB2, CyclinD1). Seventeen patients (18–44 years) were identified in database of our medical center from 2012 to 2016, 13 were male and 4 female.
Results: The investigation revealed Urobasal A subtype in 14 (82 %) cases, 10 of them were low grade non-invasive (pTa), and 4 tumours were high-grade early invasive (pT1). Urobasal B subtype was defined in one case (6 %) non-invasive, of high-grade tumour (pTa). Two cases (12 %) showed SCCL characteristics, one muscle-invasive (pT2 high grade) and one prostate-invasive (pT4a high grade). Besides, multiple recurrences and progression to T1 were detected in a 30-year-old male patient with urobasal A subtype of cancer.
Conclusion: Urothelial bladder carcinoma in early-onset patients tends to be of urobasal A molecular subtype and is associated with low pathology stage. Further investigations are needed to validate these findings.

OFP-09-006
Assessing interrater variation with funnel plots in 2,190 prostate biopsies
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Objective: Compare pathologist diagnostic rates (DRs) in prostate biopsies read over 6 years.
Method: All in house prostate biopsies read at a large teaching hospital were extracted with a previously developed custom program that uses string matching, fuzzy string matching and hierarchical pruning to categorize diagnostic information. A GNU/Octave program calculated the DRs for each pathologist and created funnel plots with the range expected due to sampling (REDS).
Results: 2,299 biopsies were extracted and >99.9 % were diagnostically categorized. Fourteen pathologists interpreted >45 cases each and together assessed 2,190. The computer categorization accuracy was estimated at 97–98 %, based on comparisons to synoptic data and human reads of 200 cases. Pathologist reproducibility varied by diagnostic category. The REDS using a 95 % confidence interval (CI) and 99.8 % CI ($P < 0.05$/ $P < 0.001$) suggest moderate agreement. The number of outliers was higher for PIN (7(95%CI)/ 4 (99.8%CI), ASAP (6/5), and WHO/ISUP grade (group) 1 cancer (WHO1) (5/3), than higher grade cancers, WHO2 (3(95%CI)/2(99.8%CI), WHO3 (3/2), WHO4 (4/2) and WHO5 (3/1).
Conclusion: Funnel plots can efficiently display volumes of information and are easily interpreted. Their use in pathology is desirable, would complement interrater variability studies and random audits, and could be used for statistically driven quality management and improvement.

OFP-09-007
t(6;11) renal cell carcinomas: A clinicopathologic and molecular study of 6 cases including two with malignant behavior. The usefulness of PAX8 and CD68 (PG-M1) immunostains in the differential diagnosis with renal pure epithelioid pecoma
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Objective: t(6;11) renal cell carcinomas (RCCs) are indolent tumours with a broad range of morphologies. The differential diagnosis include Xp11 translocation RCCs, epithelioid angiomyolipomas and common RCCs.
Method: Six primary (3 F, median age: 38 years) and two metastatic samples were analyzed by immunohistochemisty and FISH.
Results: All tumours labelled for cathepsin K and Melan-A and were negative for CD68(PG-M1). HMB45 and PAX8 were detected in 5 of 6 tumours. Four epitheliod angiomyolipomas, used as control, were positive for cathepsin K, melanocytic markers and CD68(PG-M1) and negative for PAX8. FISH results showed TFEB gene translocation in all t(6;11) RCCs with a high frequency of split TFEB fluorescent signals (mean 74 %) with increased gene copy number (3–5 fluorescent signals;

CEP6 3–4 copies) in the primary and metastatic samples of the two aggressive tumours. Thirty-four control tumours (10 clear cell RCCs, 10 papillary, 5 chromophobe, 5 oncocytomas and 4 epithelioid angiomyolipomas) showed lower percentage of split signals (mean 2 %).
Conclusion: We report the high frequency of split signals by FISH in tumours with t(6;11) rearrangement and the occurrence of TFEB gene copy number gains in the aggressive cases, analyzing either the primary or metastatic tumour. We demonstrate the usefulness of CD68(PG-M1) in distinguishing t(6;11) RCC from epithelioid angiomyolipoma.

OFP-09-008
A tissue microarray expression analysis of cell signaling pathways in recurrent non-muscle invasive bladder cancers
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Objective: NMIBC (Non-Muscle Invasive bladder cancer) has a high risk of recurrence. Recurrent tumours may acquire certain molecular alterations. We studied the differences in cell cycle pathway molecules and PDL-1 by immunohistochemistry (IHC) on tissue microarrays (TMA) in primary and recurrent NMIBCs.
Method: Using FFPE tissue, TMA of 42 NMIBC (20 primary and 22 recurrent) were constructed. IHC for p53, p21/WAF1/Cip1, Ki-67 proliferation index and PDL1 (clone E1L3N) was performed. p53 and p21 nuclear staining were expressed as semiquantitative H-score (Histo-score, range 0–300). <10 % cells showing nuclear p21 expression were considered p21-altered. PDL1 was positive when >5 % tumour cells showed membranous expression.
Results: The mean time to recurrence was 39 months (range 4–109). The difference in H-scores for p53 was significant for recurrent ($p = 0.02$) and progressive (p–0.04) tumours. Significant alteration in p21 was seen in recurrent tumours ($p = 0.04$). Loss of p21 was associated with p53 ($p = 0.03$). Ki-67 index was higher in recurrent tumours. PDL-1 expression was seen in one progressive HG MIBC (strong expression in 50 % cells).
Conclusion: Alteration in cell cycle regulators, cellular proliferation and immune tolerance is seen in recurrent NMIBCs as compared to primary tumours. Patients with low grade non-invasive bladder cancers are unlikely to benefit from anti-PD-1/PD-L1 directed therapies.

OFP-09-009
Twist and cadherin switching are markers of aggressive human prostate cancer
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Objective: Epithelial-mesenchymal transition (EMT), by reduced E-cadherin and increased N-cadherin, is a feature of aggressive tumours. Here, we examined the EMT-regulator Twist and E/N-cadherin profile in different prostatic tissues.
Method: Sections from radical prostatectomies (Haukeland University Hospital, Norway, 1986-2007) were immunohistochemically stained for E/N-cadherin ($n = 338$) and Twist ($n = 104$). Castration resistant prostate cancers (CRPC), non-skeletal metastases, skeletal metastases and benign prostatic hyperplasias (BPH) were also examined. Further, Twist mRNA data was examined for validation in a different cohort.
Results: Low E-cadherin was associated with high Gleason score, extraprostatic extension, seminal vesicle invasion, lymph node infiltration and high pathologic stage. In univariate survival analyses, high Twist, low E-cadherin and E/N-cadherin switching were strongly associated with clinical recurrence and cancer specific death, with independent prognostic impact for Twist (HR 2.7, $p = 0.002$ and HR 2.7, $p = 0.023$), E/N-cadherin switching (HR 3.3, $p = 0.001$ and HR 8.1, $p < 0.0005$), Gleason score and pathologic stage. High Twist mRNA expression was related to reduced patient survival in a validation cohort ($p = 0.001$). Twist was significantly stronger in localized cancers compared to other tissue groups. E/N-cadherin switching was not observed in BPH.
Conclusion: Twist expression and a switch from E- to N-cadherin predict aggressive human prostate cancer, reflecting the importance of EMT for clinical progress of these tumours.

OFP-09-010
Epigenetics and prostate cancer: Defining the timing of DNA methyltransferases deregulation during prostate cancer progression
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Objective: DNA methyltransferases (DNMTs) regulate gene expression by methylating cytosine residues within CpG dinucleotides. Preclinical studies have shown that DNMTs are involved in prostate cancer (PCa) progression. However, the expression of DNMTs in clinical samples across the spectrum of PCa progression has not been studied before.
Method: We examined the expression of DNMT1, DNMT2, and DNMT3b on tissue microarrays of 244 PCa (45 low-grade, 97 high-grade, 52 hormonally-treated, 40 castrate-resistant and 10 neuroendocrine carcinomas) and 100 adjacent non-neoplastic samples by immunohistochemistry.
Results: DNMT1 and DNMT2 expression was higher in carcinomas compared to non-neoplastic tissue ($p < 0.001$ and $p = 0.001$, respectively). DNMT1 expression was further upregulated in high-grade compared to low-grade ($p = 0.009$) carcinomas and in neuroendocrine compared to castrate-resistant carcinomas ($p = 0.031$). DNMT2 was upregulated in treated and castrate-resistant compared to untreated carcinomas ($p < 0.001$). DNMT3b expression was low in low-grade and high-grade carcinomas and in treated carcinomas, but was upregulated in castrate-resistant ($p < 0.001$) and neuroendocrine carcinomas ($p < 0.001$).
Conclusion: Our results reveal a differential timing of DNMTs deregulation during PCa progression. DNMT1 is gradually upregulated during the progression of PCa. DNMT3b is upregulated at late stages of PCa progression, correlating with the emergence of aggressive phenotypes, whereas DNMT2 is upregulated as a response to hormonal therapy.

OFP-09-011
The value of yolk sac and mixed histotypes in chemotherapy resistance (CTR) of testicular germ cell tumours (GCT). A study at Centro Hospitalar de São João (CHSJ), Porto, Portugal
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Objective: GCT encompass seminomatous (SGCT), nonseminomatous (NSGCT—pure-and-combined) and mixed (SGCT/NSGCT) histotypes, with therapeutic implications. Glypican-3 (GPY3) was reported to increase diagnostic accuracy of yolk sac differentiation (YSD). We aimed to evaluate the value of GPY3 in the identification of YSD, and also of mixed primary GCT as putative predictors of CTR.
Method: Re-evaluation of pathologic (histology and immunohistochemistry)-clinical features and CTR of all consecutive NSGCT/mixed histotypes ($n = 62$) diagnosed/treated at CHSJ (2005–2016). GPY3 immunohistochemistry was systematically used (0–5 fragments/case) to characterize YSD. CTR was defined as receipt of any second-line chemotherapy for non-responsive, progressive or relapsed disease or histologic evidence of viable tumour in post-chemotherapy mass excisions.
Results: GPY3 allowed identification of YSD in more 65.4 % NSGCT/mixed CGT compare to original diagnoses. CTR was observed in 19 out

of 62 NSGCT/mixed GCT (73.7 % displaying teratomatous, 52.6 % YSD components). GCT with YSD/GPY3+ (n = 26) displayed more CTR, but not significantly compare to cases without YSD/GPY3+ (n = 18). Mixed GCT (n = 17) associated significantly (p = 0,001) with CTR compare to NSGCT (n = 23).
Conclusion: Our results corroborate that GPY3 increases diagnostic accuracy of YSD. Mixed GCT (e.g, with teratomatous component) is an important predictor of CTR in testicular GCT.

OFP-09-012
Correlation between expression of epigenetic silencer EZH2 and Claudin-4 and their prognostic value in urothelial bladder cancer—immunohistochemical study
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Objective: Ezh2 transcriptional repressor has a major role in oncogenesis of the bladder. Since epigenetic mechanisms are crucial in alteration of Claudin-4 in urothelial bladder cancer (UBC), we investigated the possible correlation between Ezh2 and Claudin-4 expression and their prognostic impact.
Method: We analyzed the relationship between immunohistochemical expression of Ezh2 and Claudin-4 in 588 cases of UBC (182-Ta, 279-T1, 127-T2 tumours), included in tissue-microarrays, and clinicopathological data.
Results: High nuclear expression of Ezh2 was strongly associated with high tumour grade, advanced stage, carcinoma in situ ($p < 0.001$, respectively), and variant differentiation of UBC ($p = 0.035$). Moreover, Ezh2 was linked to hematuria and cancer specific death ($p = 0.031$, and $p < 0.001$, respectively). Ezh2 and membranous Claudin-4 staining correlated directly ($P < 0.001$). Claudin-4 exhibited association with tumour grade, stage, and recurrent disease ($p < 0.001$, $p = 0.001$, $p = 0.008$, respectively). Kaplan-Meier analyses showed that high Ezh2 expression predicted worse survival of the patients ($p < 0.001$), while Claudin-4 indicated shorter recurrence free survival ($p = 0.034$).
Conclusion: Correlation of high Ezh2 expression and strong Claudin-4 staining may suggest that Ezh2 activity has limited influence to Claudin-4 regulation. Overexpression of both Ezh2 and Claudin-4 indicates aggressive behavior of UBC. They may therefore serve as useful biomarkers for UBC and promising targets for therapy.

Tuesday, 5 September 2017, 17:15–19:15, G109
OFP-10 Joint Session: Endocrine Pathology / Infectious Diseases Pathology

OFP-10-001
Immunohistochemical evaluation of the phosphorylated AKT1 expression in well-differentiated pancreatic neuroendocrine tumours
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Objective: The Akt signaling pathway is involved in tumour cell proliferation and survival. We aimed to determine phosphorylated AKT1 (pAKT1) immunoexpression in a cohort of well-differentiated pancreatic neuroendocrine tumours (PNETs).
Method: pAKT1 status of the tumours was analyzed using an immunohistochemical analysis (IHC). Expression levels were associated with tumour characteristics and clinical outcomes.
Results: Forty-one patients (21 males, median age 57 years) with PNET Grade (G) 1 (n = 12), 2 (n = 20), 3 (n = 9) were studied. Nuclear expression of pAkt1 was detected in 8.3 % G1, 45.0 % G2, and 88.9 % G3 pNET cases. Overexpression of pAKT1 was observed most frequently in primary and metastatic pNETs G3. No correlation was found between pAkt1 expression and tumour size, lymphovascular invasion, somatostatin receptor 2A status, overall survival.
Conclusion: pAKT1 is observed in different groups of pNET patients with the highest expression levels in well-differentiated PNETs G3. The association of pAKT1 to enhanced aggressiveness and histological grade suggests its potential value as prognostic and predictive biomarker and target in PNETs.

OFP-10-002
Is it about time that liquid-based preparation substituted for conventional smear in thyroid fine needle aspiration? A systematic review and meta-analysis
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Objective: Conventional smear (CS) using fine needle aspiration cytology (FNAC) has been established as the test of choice for diagnosing thyroid lesions, despite low sample adequacy and inter-individual variations. Although a liquid-based preparation (LBP) technique has been recently applied to overcome these limitations, its clinical utility and its accuracy over CS is controversial. This study aimed to determine the true sensitivity and specificity of LBP in thyroid FNAC by meta-analysis.
Method: We searched major electronic databases (MEDLINE, Embase, Cochrane library, Google Scholar) with queries of "thyroid," "liquid-based preparation," and "liquid-based cytology." Original articles including cytohistologic correlation data comparing the accuracy of any LBP technique, such as ThinPrep, SurePath, and Liqui-Prep, with CS were included for qualitative meta-analysis and preparation of synthesized reporter operating curves (sROC).
Results: A total of 372 studies were screened and 51 original articles were eligible for full-text review; finally, 24 studies were chosen for the meta-analysis. Average sample inadequacy was significantly lower in two mainstream LBP methods (ThinPrep and SurePath) than CS. Specificity and sensitivity by sROC were similar or slightly superior for LBP versus CS. Various cytomorphologic changes by each method have been reported.
Conclusion: Although a learning curve is essential for adapting to the cytomorphologic features of the LBP technique, our results support the use of two mainstream LBPs alone in thyroid FNAC that LBP will increase the sample adequacy and reduce the workload with similar accuracy. More data and further evaluation are needed for the other LBPs to confirm they provide similar results.

OFP-10-003
Incidence of non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFPT) in a series of papillary thyroid carcinoma (PTC)
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Objective: To determine the clinical, cytological and follow-up characteristics of NIFPT in a retrospective series of PTC.
Method: Subjects: patients operated in two institutions between 2005 and march 2017 with histological diagnosis of non-invasive follicular variant of PTC or follicular-patterned neoplasm of uncertain malignant potential (FPN-UMP) due to their nuclear characteristics. Method: retrospective observational study. Variables collected: age, sex, previous cytological

diagnosis, size, type of surgery, treatment, current status, time of follow-up and tests performed during it.
Results: Of a total of 662 cases of PTC and FPN-UMP, 15 corresponded to NIFPT (2,3 %) from 14 patients, 8 males and 6 females, (one with two tumours), with ages ranging from 24 to 64. Previous cytological diagnoses were: two Bethesda I, four Bethesda II, five Bethesda III, two Bethesda IV, one Bethesda V and one Bethesda VI. Nodule size ranged from 12 to 60 mm. Total thyroidectomy was performed in 12 patients, with subsequent radioiodine treatment in 10, and hemithyroidectomy in the remaining two. All cases are alive without neoplasm. During the 77′ 75 years of cumulative follow-up, 48 thyroid ultrasounds, 13 radioiodine screenings and 102 analytical tests have been performed.
Conclusion: The conservative treatment of this entity can save on substitute treatments and unnecessary tests and therapies.

OFP-10-004
From Bern to Turin, historical aspects of the poorly differentiated carcinoma of the thyroid
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Objective: Recapitulate the history of the poorly differentiated carcinoma of the thyroid (PDC).
Method: We review the literature examining the descriptions that are found for this entity in the past. We also presented the actual proposed diagnostic criteria of PDC.
Results: The actually called PDC was first described by Sakamoto (1983) and Carcangiu (1984). Carcangiu and colleagues pointed out the distinctive growth pattern as well morphologic criteria (among others insular/solid tumour, significant mitotic activity and tumour necrosis); on the other and Sakamoto and colleagues based the diagnosis on tumour growth pattern (solid, sclerotic or trabecular). Both the authors postulated that PDC has an intermediate behavior between well differentiated and anaplastic thyroid carcinomas. Carcangiu et al. observed that this tumour was de facto identical to the Wuchernde Struma (WS) of Langhans (1907). Interestingly Wegelin (Bern, 1879-1968) recognized that features of benign thyroid trabecular adenomas in cases of WS were "exaggerated in a grotesque way". He also speculated about relationship between WS and the cases of "metastasizing adenomas" of the thyroid.
Conclusion: Turin's consensus criteria (2006) of PDC were defined based on growth pattern (solid, trabecular, or insular) and morphologic features (pleomorphic nuclei, mitoses, coagulative tumour necrosis) to allow a reproducibility of the PDC's diagnosis.

OFP-10-005
Expression of PCSK2 in neuroendocrine tumours suggest primary location of midgut and lung if found in metastasis
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Objective: Diagnosis of neuroendocrine tumours (NETs) is made from metastasis without knowledge of primary tumour location. Specific immunohistochemical (IHC) markers are needed. Proprotein convertase 2 enzyme (PCSK2) is expressed in neural and neuroendocrine cells.
Method: Tumour material consisted of 74 NETs from 12 different primary sites, and 16 primary—metastasis couples. TMA slides were stained with standard IHC protocol, validated according to biological location of PCSK2 in normal cells. PCSK2 positive NETs were further studied in larger cohorts. Adenocarcinomas from the pancreas, gastric mucosa and colorectal served as control of same organ origin.
Results: All midgut (appendix and ileum—caecum) NETs were strongly positive with PCSK2. Majority of pheochromocytomas and paragangliomas, and half of typical and atypical lung carcinoids, were positive. NETs of the thymus, gastric mucosa, pancreas, rectum, thyroid and parathyroid were negative. In metastases, staining of PCSK2 was similar to primaries. Gastrointestinal adenocarcinomas were negative, except focal positivity in some colorectal carcinomas. No correlation existed between PCSK2 and Ki-67 indicating antigen stability.
Conclusion: PCSK2 can be used in antibody panel in diagnosis of metastatic NETs. Positivity suggests primary location of midgut and lung in cytokeratin positive tumours, and pheochromocytoma—paraganglioma if cytokeratin is negative.

OFP-10-006
Neglected tropical diseases: A histopathological review
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Objective: Neglected tropical diseases (NTDs) are a diverse group of communicable diseases that prevail in tropical and subtropical condition in 149 countries, affects mainly the poor and more than one billion people. In May 2013, the 66th World Health Assembly adopted a resolution WHA66.12. Also on 28 may 2016, the 69th WHA approved a resolution recognizing mycetoma as a neglected tropical disease. Histopathological examination of tissue biopsies for infectious organism identification is an important diagnostic tool that will help the clinician in initiating therapy for these diseases.
Method: This is a 2 year prospective study of surgical specimen of NTDs carried out in a tertiary hospital in Nigeria from (March 2015–February 2017). The specimen was fixed in 10 % buffered formalin and processed with routine hematoxylin and eosin. Special stains used include Ziehl-Neelson stain, Periodic Acid Schiff and Grocott's Methylamine Silver and Gram stain.
Results: A total 35 cases of NTDs were seen during the study period out of which 30 cases were male and 5 cases were female. In the review of the 35 biopsies, the commonest diagnosis was schistosomiasis 26(74.3 %), followed by mycetoma 5(14.3 %), taenia saginata/cistecercosis 3(8.5 %) and oncocerciasis 1(2.9 %). The commonest site of occurrence of NTDs is the appendix 19(54.4 %) with the entire patient presenting with acute abdomen.
Conclusion: NTDs are still very common communicable disease in the tropics, affecting the poor in our society. We commend the World Health Assembly (WHA) for recognizing mycetoma as a NTD. We also recommend countries affected to commit to (WHA) Resolutions and WHO Road Map for NTDs.

OFP-10-007
BAP1 in paragangliomas and pheochromocytomas
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Objective: BRCA1-Associated Protein 1 (BAP1) is a tumour suppressor gene encoding a deubiquitinating enzyme involved in regulation of cell cycle, cellular differentiation, DNA damage response, and chromatin remodeling. Germline and somatic mutations of BAP1 have been associated to an increasing number of tumours. Recently, Wadt and colleagues identified a patient carrying a germline BAP1 mutation with uveal melanoma and paraganglioma. Somatic loss of BAP1 wild-type allele was detected in the paraganglioma suggesting a possible involvement of this gene in paraganglioma and pheochromocytoma pathogenesis. Aim of this study was to assess the BAP1 role in these tumours.
Method: BAP1 nuclear expression was assessed with immunohistochemistry in the FFPE samples of 21 paragangliomas and 34 pheochromocytomas. Mutational analysis of exons 1–17 of BAP1 in the same samples is in progress.
Results: BAP1 nuclear expression was lost in 3/21 (14.3 %) paragangliomas and in 20/34 (58.8 %) pheochromocytomas. Mutational

analysis will reveal if this loss of expression is due to mutations or if other molecular mechanisms must be investigated.
Conclusion: Our findings showed that loss of BAP1 nuclear expression is rather frequent in paragangliomas and pheochromocytomas, further supporting the role of this gene in these tumours.

OFP-10-008
Validity of a minimally invasive autopsy for cause of death determination in paediatric seaths from Sub-Saharan Africa
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Objective: To validate a simple and much more acceptable minimally invasive autopsy (MIA) for infectious cause of death investigation in paediatric deaths.
Method: The validity of the MIA approach in determining the cause of death (CoD) was assessed in 54 post-neonatal paediatric deaths (age range: > = 1 month–15 years) in the Maputo Central Hospital, Mozambique, by comparing the results of the MIA with those of the complete diagnostic autopsy (CDA).
Results: A CoD was identified in 52/54 (96 %) of the cases in the MIA, with infections and malignant tumours accounting for the majority of diagnoses. MIA categorization of disease showed a moderate concordance with the CDA categorization (Kappa = 0.72) and sensitivity, specificity and overall accuracy were high. The ICD-10 diagnoses were coincident in up to 75 % (36/48) of the cases. The MIA allowed the identification of the specific pathogens deemed responsible for the death in 25/32 (78 %) of all deaths of infectious origin.
Conclusion: MIA showed a substantial performance for CoD identification in this series of paediatric deaths in Mozambique. MIA could provide robust data for CoD surveillance especially in resource-limited settings, which can be helpful to guide child survival strategies in the future.

OFP-10-009
Necrotising fasciitis ("Flesh Eating Disease") due to group A streptococcus pyogenes at the University of Texas Medical Branch: 2000-2017
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Objective: Retrospective study of necrotizing fasciitis (NF) due to Group A Streptococcus pyogenes (GAS) at an academic institution.
Method: 5,780 autopsy records were searched between 2000 and 2017. Three cases of NF due to GAS were identified (2003, 2011 and 2016). Histologic sections and clinical data were analyzed. Whole-genome sequencing from the 2016 isolate was performed.
Results: All cases were confirmed by premortem blood cultures and postmortem soft tissue cultures. Lower extremities were the site of infection for all cases. In two cases, the clinical signs of NF were subtle and consisted of localized pedal and malleolar erythema and edema. One case survived for 24 hrs and the other two died within 6 hrs of admission. Histologic evidence of NF and sepsis was present in all cases. The isolate from 2011 was characterized by western immunoblotting and milkplate hydrolysis assay that revealed strong expression of secreted streptococcal cysteine protease (SpeB) that is crucial for severe tissue destruction and dissemination. Whole-genome sequencing of the isolate from 2016 revealed it to be a serotype emm77 strain that has an intact hasABC operon encoding the hyaluronic acid virulence factor. This strain also carried genes encoding superantigens SpeG and SpeK, and TetM tetracycline resistance factor.
Conclusion: NF due to GAS is rapidly progressive and highly lethal, whose initial presentation can be subtle. Deterioration occurs rapidly unless aggressive medical and surgical treatment is started promptly. These cases exemplify GAS infections with subtle clinical presentation and rapid lethal outcome due to expression of several virulence factors and superantigens.

OFP-10-010
The efficiency of a minimally invasive autopsy diagnosing a disseminated strongyloidiasis
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Objective: To demonstrate the utility and profitability of a minimally invasive autopsy in immunocompromised patients from endemic regions.
Method: A core needle autopsy was performed on a 36 years-old Guinean man with the diagnosis of AIDS. He presented nonspecific symptoms and consecutive diagnostic tests for parasitic infections had been performed, resulting repeatedly negative. After dying from acute respiratory failure, multiple cylinders were obtained from the brain, thorax and abdomen and analysed under the microscope.
Results: Disseminated strongyloidiasis was diagnosed after identifying Strongyloides stercolaris larvae in the brain, lungs and intestinal crypts, the latter being the most affected when presenting abundant eggs and larvae in different maturational states.
Conclusion: (i) A blindly, but exhaustively, performed core needle autopsy results highly efficient in patients with disseminated diseases such as AIDS. This current method proved to be extremely useful and cost-effective to identify the cause of death. (ii) False negative results in serological tests are increased in immunocompromised patients. In order to avoid a fatal end caused by an infection that has easy treatment, it is recommended to apply prophylactic treatment to patients coming from endemic regions.

OFP-10-011
How to recognise parasites in tissue sections
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Objective: With millions of refugees flooding into Europe it is important for doctors of first contact, who are usually pathologists or other Laboratory workers, to be able to identify the parasitic diseases that they will inevitably be bringing with them.
Method: Over a lifetime of dealing with Infectious Diseases the author has collected a wide range of conditions that have been documented with, as far as possible, clinical histories and photographs, ancillary investigations, gross and microscopic images. The majority of the conditions have been encountered by the author, but many have been kindly donated by pathologists from many countries in which specific diseases occur.
Results: The images have been taken in the sequence in which a practising pathologist examines every slide that crosses his or her desk; not just a single high magnification view of the causative parasite.
Conclusion: This is a Cooke's Tour through most of the human parasites that are likely to be encountered by practising pathologists.

OFP-10-012
Plurihormonal cells of normal anterior pituitary
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Objective: It is yet to be explained whether plurihormonal cells are more often found in the normal pituitary gland or in adenomas. Objective: to investigate a possible co-expression of hormones by the cells of the normal adenohypophysis in adult human autopsy material.

Method: We studied 10 pituitary glands of 4 female and 6 male (the average age was 56,5 ± 4,8 years) with cardiovascular and oncological diseases. We used the Gordon and Sweet's silver staining method, double staining immunohistochemistry with 11 hormone combinations, confocal laser scanning microscopy (CLSM) with a mixture of 5 hormones. These combinations were: prolactin /thyroid-stimulating hormone (TSH), prolactin/luteinizing hormone (LH), prolactin /follicle-stimulating hormone (FSH), prolactin/ adrenocorticotropic hormone (ACTH), growth hormone (GH)/TSH, GH/ LH, GH/FSH, GH/ACTH, TSH/LH, TSH/FSH, TSH/ACTH.
Results: We found that the same cells of the normal adenohypophysis can co-express prolactin with ACTH, TSH, FSH, LH; GH with ACTH, TSH, FSH, LH, and TSH with ACTH, FSH, LH. The comparison of the average co-expression coefficients of prolactin, GH and TSH with other hormones showed that the TSH co-expression coefficient was significantly the least (9,5 ± 6,9 %; 9,6 ± 7,8 %; 1,0 ± 1,3 % correspondingly).
Conclusion: Plurihormonality of normal adenohypophysis is an actually existing phenomenon, which refutes the concept "one cell type—one hormone", as had been accepted before.

Wednesday, 6 September 2017, 08:30–12:00, G104-G105
OFP-11 Digestive Diseases Pathology - GI

OFP-11-001
Clinical relevance of histological grading based on poorly differentiated clusters (PDC) in patients with rectal carcinoma treated with neo-adjuvant chemo-radiotherapy
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Objective: The clinical outcome of patients with locally advanced rectal cancer after neo-adjuvant chemo-radiotherapy (CRT) depends on tumour response to treatment that can be measured through tumour regression grade (TRG) and post-treatment (y) TNM stage. Currently, little is known on the prognostic relevance of pre-treatment histopathological features of rectal cancer. In this study we aimed to investigate the prognostic value of histological grading based on the counting of poorly differentiated clusters (PDC) of neoplastic cells in pre-treatment biopsies of rectal cancer submitted to neo-adjuvant CRT.
Method: Grading based on PDC counting was retrospectively applied to 204 pre-treatment endoscopic biopsies of rectal carcinomas treated with neo-adjuvant CRT and surgery.
Results: . Inter-observer agreement in the assessment of PDC grade was good (K: 0,79). High PDC grade was significantly associated with high yT stage ($P = 0{,}044$), yM+ status ($P = 0{,}0004$) and unchanged TNM stage or TNM upstaging ($P = 0{,}032$). In addition, it was a significant and independent prognostic factor for cancer specific survival (CSS).
Conclusion: Pre-treatment high PDC grade is significantly associated with low response to therapy and worse prognosis. This suggests that it might be used to discriminate potential non-responders to neo-adjuvant CRT and to design tailored therapeutic strategies for patients with locally advanced rectal cancer.

OFP-11-002
SERPINB5 overexpression and its association with CCRT resistance and prognostic importance in rectal cancers
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Objective: Due to the varying characteristics and conflicting outcomes on overall survival of rectal cancers (RCs), many studies have been undertaken to determine various prognostic and predictive factors for its mainstay treatment of CCRT followed by surgery. Cell motility of cancer cells contributes to tumour invasion, migration and eventually metastasis. However, the genes associated with cell motility (GO:0048870) had yet been systemically evaluated in RCs.
Method: A comparative analysis of gene expression profiles was applied to a transcriptomic dataset (GSE35452) with focus on genes associated with cell motility, where SERPINB5 was recognized as the most significantly upregulated. 172 primary RCs which underwent neoadjuvant CCRT followed by surgical resection were collected. Immunohistochemical study was used to semiquntatively assess the expression level of SERPINB5 protein.
Results: High immunoreactivity of SERPINB5 was significantly linked to pre- and post-CCRT advanced disease, lymphovascualr invasion, and poor response to CCRT (all $P \leq 0.015$). SERPINB5 overexpression was not only negatively associated with disease-specific (DSS), local recurrence-free (LRFS) and metastasis-free survival (MeFS) rates in univariate analysis, but also an independent prognostic factor for DSS and MeFS in RCs (all $P \leq 0.043$).
Conclusion: SERPINB5 may play an important role in RC progression and response to neoadjuvant CCRT, and serve as a novel prognostic factor.

OFP-11-003
Increased homogeneity and interobserver agreement after addition of p53 staining within a digital expert panel for Barrett's oesophagus
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Objective: Interobserver agreement for dysplasia in Barrett's oesophagus (BE) is low and guidelines advise expert review of dysplastic cases. Therefore, a digitalized review platform was set up in the Netherlands, employing 5 core BE pathologists and expanded with 10 other BE pathologists to reach extended coverage. We assessed the added value of p53-IHC on the assessment of neoplastic BE.
Method: Sixty single HE slide BE cases (20 NDBE, 20 LGD and 20 HGD) were digitalized and independently assessed by 9 BE pathologists. After wash-out time, cases were re-assessed with the addition of concordant p53-IHC slides. Outcomes were: number of IND diagnoses, interobserver agreement and accuracy of the 9 BE pathologists compared to gold-standard diagnosis.
Results: Addition of p53-IHC decreased the mean number of IND diagnoses from 10/60 to 7/60 ($p = 0.08$). Mean interobserver agreement increased significantly from 0.62 to 0.77 (dysplasia versus no dysplasia, $p = 0.0001$). Accuracy compared to the GS diagnosis increased significantly from 80 to 88 % ($p = 0.003$).
Conclusion: Addition of p53-IHC significantly improves homogeneity within the BE review panel, increases interobserver agreement and accuracy; and decreases the number of IND diagnoses. This can ultimately lead to a lower number of endoscopies and better standard of care for BE patients.

OFP-11-004
Assessment of tumour budding in lymph node and distant metastases of stage IV colorectal cancer patients
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Objective: Tumour budding (TBD) is an additional prognostic factor in colorectal cancer (CRC) based on the UICC TNM classification 2017. Data on TBD In lymph node (LN) and distant metastases (DM) in comparison to primary CRC are still missing.

Method: TBD was visualized by pan-cytokeratin staining on 73 stage IV CRC and categorized into intra- (ITB) and peri-tumoural budding (PTB), intra-(INB) and perinodal (PNB) budding and intra-(IMB) and peri-metastatic tumour budding (PMB). Overall TBD (OTB) was defined as independent of its location (OTB, ONB, OMB). For survival analysis, tumours with low and high grade TBD were subdivided by a cut-off of 10 tumour buds.
Results: Tumour bud counts were higher in primary CRC compared to LN and DM (PNB: 13; INB: 18; ONB: 21 vs PMB: 10; IMB: 21; OMB: 22 vs PTB: 23; ITB: 24; OTB: 33). Significant differences were detected between PTB/PNB ($p < 0.001$), OTB/ONB ($p = 0.008$), PTB/PMB ($p < 0.001$) and OTB/OMB ($p = 0.007$). INB, PNB and V1 were associated with PMB ($p = 0.032$, $p = 0.001$, $p = 0.003$). Patients with a high OMB number showed a trend towards a worse prognosis.
Conclusion: TBD in LN and DM is a parameter of tumour progression. The data seem to be promising for further analysis in multi-centric trials.

OFP-11-005
Glycomic profiling of pseudomyxoma peritonei reveals highly increased fucosylation of N-glycans

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Objective: Our aim was to compare the N-glycan profiles of pseudomyxoma peritonei (PMP), i.e. peritoneal mucinous carcinoma, and normal appendix, to find new potential therapy targets and biomarkers.
Method: We analyzed the N-glycan profiles from formalin-fixed, paraffin-embedded tissue blocks of 8 normal appendices, 8 low-grade appendiceal mucinous neoplasms (LAMNs), and 8 high-grade (HG) PMPs by mass spectrometry. Further, we analyzed the expression of fucosylation-related enzymes and fucosylated glycans by immunohistochemistry and lectin histochemistry, and, finally, studied the relationship between fucosylation and MUC2 expression by cell culture experiments.
Results: The N-glycan profiles of PMP tumours clearly differed from those of normal appendices and principal component analysis using all the significantly differing monosaccharide compositions separated the samples into distinct groups (control, LAMN, HG). Especially increased fucosylation was prominent in the tumours' N-glycans. In line with that, four fucosylation-related enzymes were upregulated in PMP tumours, when analyzed using microarray expression analysis. By immunohistochemistry, these enzymes were localized into PMP tumour cells. Finally, we could demonstrate relationship between fucosylation and GNAS mutation-induced MUC2 upregulation in colon adenocarcinoma cell line HCT116.
Conclusion: Highly increased fucosylation is the most prominent N-glycosylation alteration in PMP tumours and it may contribute to the highly upregulated mucin production.

OFP-11-006
Tumour budding according to the International Tumour Budding Consensus Conference (ITBCC) recommendations strongly predicts disease-free survival in stage II colorectal cancer

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Objective: Tumour budding is a strong and independent prognostic factor in colorectal cancer (CRC). The International Tumour Budding Consensus Conference (ITBCC) established a set of recommendations for assessing and reporting tumour budding in CRC. The aim of this study was to test the ITBCC method in Stage II CRC.
Method: In 151 Stage II CRC patients, budding was assessed on scanned slides according to ITBCC. Cutoffs were: low (Bd1): 0–4 buds, intermediate (Bd2): 5–9 buds, high (Bd3): ≥10 buds. Associations with disease free survival (DFS) and overall survival (OS) were examined. 20 cases were assessed by a second observer.
Results: 43.1 % of cases were Bd1, 27.2 % Bd2 and 29.8 % Bd3. Each additional bud was associated with poorer OS in univariate analysis ($p = 0.0386$, HR 1.048, 95%CI 1.002–1.095). For 3- and 5-year DFS, Bd3 showed worse survival versus Bd1/2 ($p = 0.0031$ and $p = 0.0025$, respectively), remaining significant in multivariate analysis for DFS ($p = 0.006$, HR 3.293, 95%CI 1.66-6.53). K-values for Bd categories were 0.73 (simple) and 0.8 (weighted).
Conclusion: High grade tumour budding (Bd3) assessed by the ITBCC method in Stage II CRC shows a detrimental adverse impact on DFS versus Bd1/Bd2. Tumour budding according to ITBCC should be included in CRC reporting guidelines.

OFP-11-007
The automatic extraction and categorisation of 22,760 stomach biopsy specimen parts from 110,970 free text pathology reports to assess Helicobacter pylori diagnostic rates

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Objective: To assess inter-observer variability in Helicobacter pylori (HP) detection rate using big data.
Method: A custom computer program was used to extract information from 6 years of free text pathology reports at a large academic center. Diagnostic information from all stomach biopsies were categorized using keyword searches, an approximate string matching library (google-diff-match-patch), and hierarchical pruning. Diagnostic rates for HP were calculated for all pathologists reporting >200 specimen parts.
Results: 22,760 stomach biopsy specimen parts were extracted from 110,970 pathology reports, >99 % of cases were categorized, and accuracy (in 200 pathologists/authors audited parts) was ~98 %. Sixteen pathologists interpreted 218–2546 and total of 22,176 specimen parts. Mean diagnostic rate for HP was 9.2 %. Twelve of sixteen pathologists had HP call rates within two standard deviation of the mean, while one pathologist was an outlier (outside the 99.8 % confidence interval, $P < 0.001$). Two pathologists not using upfront special stains for HP had diagnostic rates within the expected range.
Conclusion: Automatic extraction and categorization of diagnostic information from free text pathology reports can be used to monitor pathologist diagnostic rates using large samples as a quality control measure. Our study reinforces Gastrointestinal Pathology Society consensus statement that upfront special stains for HP are unnecessary.

OFP-11-008
RAS Registry: Molecular pathological analysis of RAS mutations in mCRC

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Objective: The RAS proto-oncogene family is frequently mutated in tumours of patients with metastatic colorectal cancer and is predictive for therapeutic success of systemic anti-EGFR-therapy. Therefore, determining the RAS status of the tumour prior to therapy is essential. In Germany, RAS testing has been validated by nationwide round robin tests organized by the Quality Assurance Initiative in Pathology (QuIP) resulting in certification of test centers. Aim of the RAS registry is to comprehensively analyze real-life diagnostic RAS testing performance by QuIP-certified centers.

Method: The RAS Registry is a prospective cohort study designed to collect real-life data (logistic parameters, test methods used, frequency and distribution of various KRAS/NRAS mutations) from QuIP-certified centers.
Results: From 2014 to 2016 data of 2,510 tumour samples with RAS mutation analysis across 27 centers were collected and analyzed. The median lab turnaround time (TAT) was 5 working-days, whereby 72 % of the results were transmitted under 6 and only 8 % over 10 working-days. Analyses of mutation frequency so far show that 55 % of samples harbor RAS mutations (48 % KRAS, 7 % NRAS).
Conclusion: This study shows that all QuIP-certified centers adhere to a median TAT of 5 working-days. The RAS mutation frequency of approx. 55 % is in line with previous studies.

OFP-11-009

Tumour-stroma ratio combined with vascular invasion improves survival prediction for colon cancer patients

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Objective: The tumour-stroma ratio distinguishes between stroma-high and stroma-low patients. Colon cancer patients with a high stroma percentage within the primary tumour have a poor prognosis, as do patients with vascular invasion. The goal of this study was to investigate whether a combination of these two parameters improves prognostic value.
Method: Tissue samples from the most invasive part of the primary tumour of 925 patients participating in the QUASAR2 trial were analyzed for tumour-stroma ratio (TSR) and the presence of vascular invasion. Stroma-high (>50 %) and stroma-low (≤50 %) groups combined with presence or absence of vascular invasion were evaluated with respect to survival.
Results: A correlation was observed between TSR and vascular invasion (χ2-test $p = 0.043$). Disease free survival (DFS) in patients with a stroma-high tumour with vascular invasion was lower compared to patients with a stroma-high tumour or a tumour with vascular invasion alone (5-yrs DFS 57 % (HR 2.4) versus 65 % (HR 1.5) and 64 % (HR 1.6) respectively).
Conclusion: Both the tumour-stroma ratio and the presence of vascular invasion are strong individual prognosticators. Combining these two parameters stratifies patients at risk for developing recurrence of disease or metastasis even further, which might have consequences for treatment.

OFP-11-010

MicroRNA expression profiling for prediction of resistance to neoadjuvant radiochemotherapy in squamous cell carcinoma of the oesophagus

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Objective: MicroRNA have been shown to play an important role in cancer biology and therapy response. Neoadjuvant radiochemotherapy followed by surgery is a standard treatment for locally advanced esophageal squamous cell carcinoma (ESCC). However, a subset of patients does not respond to RCTX. In the present study we evaluated whether miRNA expression profiling can predict resistance to RCTX in ESCC.
Method: 54 patients with ESCC (cT3-4, cN1-3, M0-1) underwent RCTX (cisplatin, 5-fluorouracil, 30-45 Gy) followed by esophagectomy. Tumour response was evaluated by histopathological tumour regression. MiRNA profiling was done using Agilent Human Microarray platform (Release 16.0) on 31 FFPE pretherapeutic biopsies (15 responders and 16 non-responders), followed by real-time quantitative PCR (QRT-PCR) in an collective of 54 patients.
Results: MiRNA profiles within and between non-responders and responders were highly similar ($r = 0.96$, 0.94 and 0.95), indicating a generally homogenous miRNA profile in ESCC. However, 12 miRNAs were differentially expressed in non-responders (>2-fold; $p \leq 0.025$). In particular, non-responders showed an upregulation of eight miRNAs (miR-1323, miR-3678-3p, hsv2-miR-H7-3p, miR-194*, miR-3152, kshv-miR-K12-4-3p, miR-665 and miR-3659) and a downregulation of four miRNAs (miR-126*, miR-484, miR-330-3p and miR-3653). QRT-PCR analysis confirmed microarray findings for miR-194* and miR-665, and ROC analysis for response to treatment showed AUC values of 0.811 and 0.817, respectively.
Conclusion: Our results indicate that miRNAs are involved in therapy response and suggests that miRNA profiles could be used to predict response to RCTX.

OFP-11-011

The phenotypic heterogeneity of Hereditary Diffuse Gastric Cancer (HDGC). Report of one family with early-onset disease

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Objective: The time-course of the development of clinically significant HDGC is unpredictable. Little is known about the progression from preclinical, indolent lesions to widely invasive, aggressive phenotypes. We report a HDGC family with a pathogenic germline CDH1-mutation (c.1901C>T) with early-onset disease, to discuss mechanisms behind morphological and clinical heterogeneity.
Method: Endoscopic biopsies from the proband (18-year-old male with widely invasive, metastatic DGC) and prophylactic total gastrectomies (PTGs) from six family members were studied by morphology and immunohistochemistry for E-cadherin, Ki-67, p53, pSrc and pStat3. Helicobacter pylori (H. pylori) cagA status was also determined.
Results: The aggressive DGC from the proband was characterised by pleomorphic cells, absent E-cadherin expression, high Ki-67 proliferation index, and p53, pSrc and pStat3 overexpression. The 6 PTGs contained early DGCs ($n = 1$–33) with typical signet-ring cells, decreased membranous E-cadherin expression and absence of p53 and Ki-67 immunoreactivity. H. pylori cag-A-positive strains were detected in all family members, except in a 14-year-old female.
Conclusion: The results of this study reinforce our previous data [Adv Exp Med Biol. 2016; 908: 371] on heterogeneity of HDGC and demonstrate that the aggressive phenotype is characterised by increased proliferation and activation of oncogenic events. The role of H. pylori infection and virulence-associated genes is debatable.

OFP-11-012

Significance of tumour-infiltrating lymphocytes (TILs) in gastric carcinomas: Association of PD-L1 and PD-1 expression with prognostic parameters and survival

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Objective: To evaluate the correlation of PD-L1 and PD-1 expression with prognostic parameters and survival in a large and well-characterized cohort of gastric carcinomas.
Method: Immunohistochemical expression of PD-L1 and PD-1 in tissue array blocks prepared from 220 gastric carcinomas were correlated with prognostic parameters comprising tumour type, TNM stage, tumour grade, lymphovascular and perineural invasion, tumour budding and survival.
Results: Of the 220 cases, included in the study, 96.4 % received adjuvant therapy comprised of 5-florouracil + folinic acid + radiotherapy. Positive

PD-L1 and PD-1 expression were observed in 12.5 % (24/192) and 88.8 % (167/188) of the cases, respectively. The majority of tumours were T3 (79.8 %), N1 (40.1 %) and M0 (90.6 %) while lymphovascular and perineural invasion and tumour budding were observed in 74.1 , 65.5 and 16.8 % of the tumours, respectively. PD-L1 expression in TILs significantly correlated with M1-stage ($p = 0.042$) whereas PD-1 expression in TILs significantly correlated with perineural invasion ($p = 0.002$). Cases with PD-L1 expression presented with a better median overall survival of 69.4 ± 16.7 months compared to PD-L1 negative tumours with a survival of 19.8 ± 2.5 months ($p = 0.0058$).
Conclusion: Our results suggest that PD-L1 expression in gastric carcinomas may be associated with favorable tumour prognosis and that tumour microenvironment including TILs should be routinely evaluated.

OFP-11-013
Olfactomedin 4 (OLFM4) expression predicts nodal status in patients with oesophageal adenocarcinoma
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Objective: Endoscopic surgery is increasingly applied for early esophageal adenocarcinoma (EAC) without lymph node metastasis (LNM). OLFM4, an intestinal stem cell marker, is correlated with metastasis in a variety of cancers. This study investigates the predictive value of OLFM4 for LNM in EAC.
Method: OLFM4 expression was evaluated immunohistochemically in 115 patients with advanced (pT2 or higher) EAC, treated by esophagectomy alone in which at least 12 lymph nodes where retrieved (pN0 $n = 24$ vs. pN+ $n = 91$). Clinicopathological factors and low (defined as less than 30 % positive tumour cells) OLFM4 expression were subjected to logistic regression and Cox regression analysis to assess prognostic value.
Results: Low OLFM4 expression correlated with tumour grade ($p = 0.01$), LNM ($p = 0.023$), and recurrence ($p = 0.019$). Furthermore, low OLFM4 (OR 3.08, 95 % CI 1.04-9.14, $p = 0.043$) was identified as an independent predictive factor for LNM in EAC. However, OLFM4 was not predictive for overall or disease free survival.
Conclusion: Loss of OLFM4 expression is independently predictive for LNM in advanced EAC, but not for survival. Further studies on endoscopically treatable early EAC are required to evaluate the potential value of OLFM4 for risk stratification of patients suitable for endoscopic vs. conventional surgery.

OFP-11-014
Tumour-budding evaluated on cytokeratin stained sections in stage II colon cancer patients, a population based study
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Objective: Tumour-budding denotes the detachment tumour cells from the adenocarcinoma bulk, either individually or gathered in small aggregates (max. 5 cells). Several studies have stated the prognostic value of tumour-budding in patients with colorectal cancer. Upcoming guidelines base scoring of tumour-budding on HE sections, despite a well-known fragility of the reproducibility.
Method: The study included all patients ($N = 589$) diagnosed with stage II colon cancer in Denmark in 2003. Tumour-budding was defined as the presence of at least 10 buds at ×200 magnification, using a paired set of HE and Cytokeratin-20 stained sections from each case. Results were evaluated regarding Recurrence-Free Cancer Specific Survival (RF-CSS) and Time-To-Recurrence (TTR).
Results: By the use of CK-20, an additional 66 patients (146 in total) were classified with budding compared to the 80 patients identified, using HE sections. Patients with tumours displaying tumour-budding by CK-20 had a significant worse prognosis of RF-CSS and TTR in both univariate (RF-CSS: HR = 1.94 (1.27–2.96), $p = 0.0009$; TTR: HR = 2.31 (1.39–3.84), $p = 0.0004$), and multiple COX-analyses (RF-CSS: HR = 2.51 (1.64–3.83), $p < 10\text{-}5$; TTR: HR = 2.87 (1.71–4.80), $p = 0.0001$).
Conclusion: Immunohistochemistry enhances detection of tumour-budding compared to HE-sections, and provides improved prognostic impact in stage II colon cancer patients.

OFP-11-015
MicroRNA-21 expression in budding colon cancer cells—multiplex stained slides analysed by confocal scanning microscopy
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Objective: Expression of microRNA-21 (miR-21) in stromal fibroblastic cells in colorectal cancers is well documented, whereas miR-21 expression in tumour budding cells is poorly described. Budding tumour cells possess increased metastatic properties and characteristics of epithelial to mesenchymal transition.
Method: To characterize miR-21 budding cells, we first developed a multiplex fluorescence staining method by combining miR-21 in situ hybridization with immunohistochemical staining for cytokeratin and laminin-gamma2, and stained 20 colon cancer cases (stage II, $n = 7$, stage III, $n = 13$). We then employed a confocal scanning microscope to obtain digital images covering the invasive front.
Results: The high resolution of the confocal digital images allowed detailed examination of the 4-fluorophore-stained slides e.g. in the discrimination of epithelial cells from adjacent stromal cells. Five out of 16 successfully processed cases had more than 10 % miR-21 positive budding cells and were all stage III cancers, and generally laminin-gamma2 negative. The presence of miR-21 in the tumour budding cells was not associated with the level of tumour budding.
Conclusion: These observations suggest that the miR-21 expression in tumour budding cells increases with cancer progression and is independent of laminin-gamma2. The confocal digital images were crucial for unambiguous examination of the complex staining patterns.

Wednesday, 6 September 2017, 08:30–12:00, Emerald Room
OFP-12 Joint Session: Pulmonary Pathology / Thymic and Mediastinal Pathology

OFP-12-001
Expression of DcR3 in lung adenocarcinoma: Clinicopathological correlation with 461 cases
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Objective: Decoy receptor 3 (DcR3) has been reported to be expressed in many malignant tumours. However, the role of DcR3 expression in lung cancer, particularly adenocarcinoma, has not been well studied in the past. In this study, we sought to investigate the expression profile and the clinicopathological implications of DcR3 expression in lung adenocarcinoma.
Method: Immunohistochemistry was used to examine DcR3 expression in lung adenocarcinoma tissue ($n = 461$). The differences in DcR3 expression among the various histopathologic patterns were analyzed. The relationship between DcR3 expression and clinicopathological

parameters, including epidermal growth factor receptor (EGFR) mutation, were also investigated.
Results: DcR3 expression was more frequently expressed in solid, acinar, and micropapillary patterns ($p < 0.0001$). Moreover, DcR3 expression was more often observed in tumours with wild type EGFR status ($p = 0.025$). In addition, DcR3 expression portends a less favorable disease-free survival in stage I patients.
Conclusion: The expression of DcR3 might be involved in the differentiation and progression of lung adenocarcinoma, and are more often expressed in EGFR wild type tumours. Therefore, DcR3 may be applied clinically for prediction of tumour progression in lung adenocarcinoma, and its inhibition may potentially be beneficial for EGFR wild type tumours.

OFP-12-002
Prognostic and predictive value of loss of nuclear RAD51 immunoreactivity in resected non-small cell lung cancer patients
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Objective: We aimed for assessing the prognostic and predictive value of loss of nuclear RAD51 immunoreactivity ('RAD51 loss') in 2 independent cohorts of stage I-III non-small cell lung cancer (NSCLC) patients, undergoing surgical resection and eventual perioperative chemo-/radiotherapy (CT/RT).
Method: The discovery set included 69 evaluable patients, 45/69 (65.2 %) with additional platinum-based CT. The replication set entailed 845 evaluable patients, 308/845 (36.5 %) with platinum based CT or RT. RAD51 loss was defined as ≤20 % of tumour cell nuclei having any nuclear RAD51 expression.
Results: RAD51 loss was observed in 40/69 (58.0 %) and 439/845 (51.9 %) evaluable tumours in the discovery and replication set, respectively ($p = 0.34$). It was more frequent in ADC compared to SCC (57.2 % vs 47.4 %, $p = 0.003$). RAD51 loss was significantly associated with worse OS in both the discovery (adjusted HR = 2.39, $p = 0.039$) and replication set (adjusted HR = 1.31, $p = 0.008$). The unfavourable prognostic effect of RAD51 loss seen in the overall population was not observed in patients receiving perioperative CT (adjusted HR = 1.07, $p = 0.73$) or perioperative RT (adjusted HR = 1.05, $p = 0.82$).
Conclusion: RAD51 loss has an unfavourable prognostic impact in NSCLC patients undergoing curative surgical resection, but it may have a favourable predictive value in the subgroup of patients receiving perioperative platinum-based CT or RT, most likely as a consequence of deficient DNA repair.

OFP-12-003
Idiopathic versus secondary Usual Interstitial Pneumonia (UIP) pattern in a series of 96 consecutive surgical lung biopsies: The value of histologic ancillary findings into a multidisciplinary discussion
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Objective: Idiopathic Pulmonary Fibrosis (IPF) is characterized by UIP pattern at histology, however several interstitial diseases may show UIP pattern. The aim of this study is to evaluate the role of ancillary histologic findings in discriminating IPF from secondary UIP.
Method: Clinical and serological data, imaging pattern, histological findings (presence/absence of honeycombing, fibroblastic foci, smoking-related interstitial fibrosis, giant cells/granulomas, bronchiolocentric damage, "bridging fibrosis", lympho-plasmacellular infiltrates, follicles, eosinophils, chronic pleuritis, bone/adipocytic/muscle metaplastic tissue, alveolar proteinosis-like material) and the confidence in the pathologic diagnosis of idiopathic or secondary UIP were collected from 96 consecutive patients undergoing surgical lung biopsy.
Results: Overall, there were 71 males and 25 females with a median age of 64 years. Fifty-one were current or former smokers.Positive serological autoimmunity tests were observed in 13 patients (13,5 %). At histology, 83 % of cases showed honeycombing changes, while fibroblast foci and patchy fibrosis were present in all cases. Giant cells/granulomas, peribronchiolar metaplasia, "bridging fibrosis", lympho-plasmacellular infiltrate, follicles with germinal centers and eosinophils were present in 33 , 43 , 32 , 50 , 7 and 6 %, respectively. Chronic pleuritis, metaplastic tissue and alveolar proteinosis-like material were detected in 5 , 50 and 16 % of cases, respectively. Identification of ancillary findings changed the diagnosis of IPF from 85 to 67 %. Chronic hypersensitivity pneumonitis increased from 12 to 23 % and collagen-vascular-disease from 2 to 6 %.
Conclusion: UIP is the most common pattern among interstitial lung disease, but a subset of patients with UIP pattern has a secondary disease. Identification of histologic ancillary findings is significantly ($p < 0.001$) associated with secondary UIP.

OFP-12-004
Pulmonary pathology of Birt-Hogg-Dube (BHD) Syndrome
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Objective: Birt-Hogg-Dube syndrome (BHD) is a newly emerging hereditary disorder caused by FLCN germline mutation. Most patients have pulmonary cysts; however, the lung specimens are often misdiagnosed as blebs/bullae or emphysema. The aim of the study is to clarify histopathologic clues to diagnosis of BHD lung.
Method: We investigated FLCN mutations and clinicopathologic findings of 400 patients from 156 Japanese BHD families. Seventy-four lung specimens were analyzed with immunostaining, Western blotting, FISH/CISH and DNA sequencing.
Results: Microscopically, each pulmonary cyst tended to be incorporated into the bronchovascular bundle and/or interlobular septum in part, and with normal-looking parenchyma in the other part. The cysts preferentially expanded the visceral pleurae. The inner surface of the cyst is lined by attenuated benign-looking pneumocytes. Type II pneumocyte-like cuboidal cells were often observed in part. Cyst-lining cells were positively stained for phospho-mTOR and phospho-S6. There were 15 neoplastic lung lesions in 8 patients; 5 adenocarcinomas, 8 atypical alveolar hyperplasias, a micronodular pneumocyte hyperplasia (MPH)-like lesion and an inflammatory myofibroblastic tumour. Four adenocarcinomas and a MPH-like lesion showed loss of heterozygosity of FLCN.
Conclusion: Pathologists should carefully distinguish BHD-associated pulmonary cysts from other lung diseases. Possible association between pulmonary neoplasms and FLCN insufficiency needs further investigation.

OFP-12-005
Predictive value of CD44v/CD24 expression in early stages pulmonary adenocarcinomas
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Objective: In the last decade the study of Cancer Stem Cell (CSCs) markers has become increasingly important in patients with solid tumours. This is of particular relevance in early stages NSCLC, where CD24 and CD44 have demonstrated promising results as prognostic

markers. Previous studies suggested that the CD44+ / CD24– phenotype defines a distinct subgroup of NSCLC. Here, we study the prognostic value of these 2 markers in early stage pulmonary adenocarcinomas (ADC).
Method: 83 pulmonary ADC (stages I and II, N0) were included. Using TMAs, IHC expression of CD44v and CD24 was studied (cut-off values ≥10 %). Results were correlated with clinical and pathological information. Overall survival (OS) and disease-free survival (DFS) estimates were determined from Kaplan-Meier analysis and compared using the log-rank test.
Results: Fifty-four percent of cases were positive for CD44v and 46 % for CD24. CD24 expression correlated with better DFS ($p = 0{,}021$), while positive CD44v cases exhibited a tendency for worse DFS ($p = 0{,}11$). By combining this phenotype, the cohort was divided in 3 different prognostic groups: "good", "intermedial" and "bad", with DFS of 120, 93 and 55 months, respectively ($p = 0{,}007$).
Conclusion: Our findings show that the CD44+ / CD24– phenotype allows the stratification of pulmonary ADC in prognostic subgroups. The possibility of using IHC as a means of predicting relapse risk in a subgroup of NSCLC in early stages is a very attractive option that deserves further investigation.

OFP-12-006
Association of molecular status and anatomic sites of metastases at diagnosis of non-small cell lung cancer (NSCLC)
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Objective: To assess the association between molecular status and anatomic sites of metastases at diagnosis in a nationwide stage IV NSCLC cohort.
Method: All non-squamous NSCLC from 2013 that were stage IV at diagnosis, without a recent history of cancer, were retrieved from the Netherlands Cancer Registry and matched to the Dutch Pathology Registry (PALGA). Four molecular subgroups were identified: EGFR+, KRAS+, ALK+, and triple-negative. For each metastatic site, proportions of tumours metastasized to this site were, per molecular subgroup, compared to the triple-negative subgroup in multivariable logistic regression analysis, taking clinicopathological variables into account.
Results: 2906 tumours were retrieved and included for analysis were: EGFR+ ($n = 222$), KRAS+ ($n = 784$), ALK+ ($n = 42$) and triple-negative ($n = 1101$). Compared to the triple-negative tumours, EGFR+ tumours had significantly more often metastasized to the bone (OR 2.14, 95 % CI 1.59-2.88) and pleura (1.56, 1.12-2.17), and less often to the adrenal gland (0.48, 0.30-0.78). KRAS+ and ALK+ tumours had significantly more often metastasized to the lung (1.34, 1.08-1.68) and liver (2.15, 1.03-4.46), respectively, than the triple-negative tumours.
Conclusion: NSCLC molecular status is associated with biological behavior. To anticipate on skeletal-related events, screening all EGFR+ patients for bone metastases is worth considering, as 49.1 % of stage IV EGFR+ patients had bone metastases.

OFP-12-007
Overexpression of endoplasmic reticulum (ER) stress molecules, XBP1s and GRP78, were associated with poor prognosis in pulmonary adenocarcinoma
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Objective: Endoplasmic reticulum (ER) stress is complicatedly involved in the development and progression of tumour by playing both protumourigenic and anti-tumourigenic roles. However, the status and clinicopathological implication of ER stress remain unclear in pulmonary adenocarcinoma (pADC). We addressed this issue.
Method: Expression of an ER chaperone molecule, GRP78, and the nuclear expression of XBP1s (XBP1 short-form), suggestive of activated IRE1a pathway following ER stress, were evaluated in patients with pADC ($n = 369$) using immunohistochemistry.
Results: XBP1s and GRP78 overexpression was detected in 10.6 % (39/369) and 17.3 % (63/365) of patients, respectively. XBP1s and GRP78 overexpression were positively correlated with each other ($P = 0.014$). The mean age of patients with XBP1s overexpression was significantly younger than those without XBP1s overexpression. XBP1s overexpression was more common in ALK-translocated pADCs compared to those without ALK translocation ($P = 0.014$). In survival analysis, XBP1s overexpression and combined XBP1s and GRP78 overexpression were significantly associated with short progression-free survival in all patients with pADC ($P = 0.026$ and $P = 0.024$, respectively) and in those with ALK-translocated pADC ($P = 0.001$ and $P < 0.001$, respectively).
Conclusion: XBP1s and GRP78 are variably expressed in pADC and related with poor prognosis when it overexpressed. ER stress pathway could be a prognostic biomarker and potential therapeutic target in pADCs.

OFP-12-008
Pleuropulmonary blastoma: A case series from a Tertiary Center
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Objective: Pleuropulmonary blastoma (PPB) is a potentially aggressive, rare childhood neoplasia. We aimed to determine correlations between histopathological features and survival in PPB patients.
Method: Records at our institution were reviewed for PPB cases, covering a 20-year period. We documented histopathological and clinical characteristics including survival data.
Results: Thirteen children (6 males, 7 females) with a mean age of 30.5 months (range, 6–83 months; 5 ≤ 2 years) were included in the study. Initial histology was Type I in 6 (46.2 %), Type II in 4 (30.8 %) and Type III in 3 (23.1 %) cases. Only cases with Type II-III histology (4/7, 57.1 %) showed anaplasia (Type I vs. Type II-III, p = 0.07). Median follow-up was 23 months (2–216). Overall survival and progression-free survival (PFS) rates were 81.8 and 36.4 %, respectively. Progression was seen in 60 % (3/5) of Type I and 66.7 % (4/6) of Type II-III cases. Among three Type I cases with progression, recurrent or metastatic tumours showed Type II histology in 1 case and Type III histology in 2 cases. Children ≤2 years of age exhibited better PFS than children >2 years ($p = 0.033$). Two patients died of disseminated disease.
Conclusion: PPBs tend to show recurrence or metastasis, especially for patients over 2 years of age.

OFP-12-009
External quality assessment of PD-L1 expression scoring based on tissue microarrays and cross-validation with whole sections method, in patients with resected, stage I-III, non-small cell lung cancer: The ETOP Lungscape project
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Objective: In this project, we harmonized ETOP laboratories' PD-L1 expression scoring on Tissue Microarrays (TMAs), by an external quality

assessment (EQA) program and cross-validated the TMA approach versus whole sections (WS), in the Lungscape cohort.
Method: PD-L1 expression was assessed on TMAs using the DAKO 28-8 IHC assay. Samples were analyzed under the same protocol. EQA was performed in two rounds. Initially, centers evaluated TMAs from four cell lines and eight tissues. Subsequently, centers' scoring was further harmonized using both the TMAs and 65 slides (DAKO-pathologist scoring available as benchmark). Cross-validation of PD-L1 scoring between TMAs and WS was performed in a randomly selected sample of the ETOP cohort. Positivity cut-off points considered: ≥1 , 5 and 50 %.
Results: EQA analysis showed that scoring was reliable, with restricted deviations from mode values, and no systematic bias. In the ETOP cohort, PD-L1 expression was available for 2182 patients, 51 % adenocarcinomas. Prevalence for 1/5/50 % cut-offs and 95%CIs were: 43 % (41–46)/34 %(32–36)/17 %(15–18). Range of >1 % prevalence among centers was 9–63 %. Setting WS as gold standard, TMAs' sensitivity and specificity for 1/5/50 % cut-offs were: 79/85/79 % and 90/93/98 %.
Conclusion: EQA showed good performance and TMAs seem a promising alternative to WS method for PD-L1 assessment.

OFP-12-010
miRNA dysregulation in chronic lung allograft rejection
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Objective: Recent evidence links miRNA dysregulation with fibrogenic disorders, including bronchiolitis obliterans syndrome (BOS), the main phenotype of chronic lung allograft dysfunction. We validated in BOS tissue samples a panel of miRNAs identified by a previous computational analysis as involved in the pathogenesis of lung fibrotic processes.
Method: The expression of miR-21, miR-34a, miR-145, miR-146b-5p, miR-381, miR-15a, and miR-let7-d was analyzed by qt-PCR and in situ hybridization (ISH) on 12 BOS samples in comparison with normal lung tissue.
Results: With qt-PCR, only miR21 and miR34a were significantly upregulated in BOS samples. ISH showed that all evaluated miRNAs were strongly expressed in fibroblasts and myofibroblasts of BOS and of vascular obliterative proliferations, while in normal lungs all miRNAs but miR21 were expressed in epithelia, endothelia and inflammatory cells.
Conclusion: The in situ and quantitative approaches were usefully integrated to highlight levels and cell specificity of miRNA expression. While qt-PCR showed increased levels of only miR-21 and miR-34a, ISH documented a possible involvement in BOS of all miRNA identified by the computational analysis, by showing their overexpression in lesional cells. Our approach suggest that miR21, the only one expressed de novo in transplanted lung, and specifically in BOS fibroblasts, represents a potential target for therapeutic silencing.

OFP-12-011
Transbronchial biopsy adequacy and sample size in a multidisciplinary team approach to interstitial lung diseases: A two-years Padova experience
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Objective: Interstitial lung diseases (ILDs) are a group of pathological processes affecting the lung interstitium. A confident diagnosis is achieved by a multidisciplinary team (MdT). Transbronchial biopsy (TBB) receives a weak recommendation in current diagnostic guidelines. Emerging data suggest an increased role for TBB. We describe our experience evaluating the factors which can impact on its adequacy.
Method: We reviewed 74 patients with clinical suspicious for ILD that underwent TBBs in our center over 2 years. For each sample we evaluated fragment number and surface area by using morphometric analysis. We evaluated and scored blood extravasation and crush artifact as partial and complete. Samples composed of vessels, bronchus or pleura were considered inadequate. A two-year follow-up was obtained to confirm the diagnosis.
Results: TBBs were diagnostic in 66/74 (89.2 %) while 8/74 (10.8 %) were inadequate. The most frequent diagnoses were organizing pneumonia (37.9 %) and usual interstitial pneumonia (21.2 %). Neither the difference in number nor in surface was statistically significant between the inadequate and diagnostic group. Crushing artifact was significantly present in all inadequate samples and in 74.2 % of adequate ones ($p = 0.034$).
Conclusion: Adequate TBBs could be successful in achieving a confident diagnosis in suspected ILD. Crushing is the parameter which impacts the most.

OFP-12-012
Transbronchial biopsy 3 weeks after lung transplantation for graduating allograft acute rejection: A clinicopathological study
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Objective: Three weeks after a lung trasplant, a transbronchial biopsy is done to graduate acute lung allograft rejection. The objective of this study is to revise the grade of acute rejection in our patients and the clinicopathological correlation.
Method: We revised 73 transbronchial biopsies 3 weeks after lung trasplantation from 2015 to 2017 and the clinical history of those patients.
Results: In 34 (46,58 %) of them we didn't identify acute rejection (A0), in 5 (6,85 %) we could see minimal acute rejection (A1), in 25 (34,25 %) we could diagnose mild acute rejection (A2) and in 9 (12,33 %), we could identify moderate acute rejection (A3). Only four patients have symptoms of acute rejection (three of them had an A2 grade and one, an A3 grade). The rest of the patients didn't have any symptoms in spite of having histological sygns of acute rejection but these patients were carefully observed and were given more immunosupressant drugs.
Conclusion: Transbronchial biopsy done 3 weeks after the trasplant is very important to identify the presence of acute allograft rejection because patients in spite of not having symptons they can be benefited of a immunosupressant prevention treatment, before the rejection symptons appear.

OFP-12-013
Iron Pill aspiration bronchitis—cytologic and histologic findings of a potential life-threatening airway injury
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Objective: Report a case of bronchial injury by iron-pill-aspiration (IPA) during oral iron supplementation. To define its cytological and histologic findings.
Method: A 91-year-old male presented to the emergency department with dyspneia, fever and vomiting. He had a previous history of lung trauma. Serum inflammation markers were elevated. Chest X-ray demonstrated lower right lobe condensation and pleural effusion. He received antibiotics and oral iron supplementation. Due to worsening of symptoms and imaging findings, bronchoscopy was performed revealing a friable, necrotic bronchial mucosa.
Results: Biopsy examination revealed extensive eroded bronchial mucosa, sloughed epithelium with deposits of coarsely, fibrillar, golden-brown deposits highlighted by Perls (iron) stain. Bronchial aspirates revealed necro-inflammatory exudates involving golden-brown fibrils. A

diagnosis of IPA induced bronchitis was assumed based on morphology and clinical information.
Conclusion: IPA bronchoscopy findings are non-specific and the differential diagnosis includes airway trauma, infections and neoplastic diseases. Histologically, direct iron-pill damage is characterized by crystalline, fibrillary, golden-brown iron deposits in necrotic epithelium which can also be identified in bronchial brushings or aspirates. Albeit rare, IPA has potential severe complications such as haemoptysis and bronchial stenosis. This entity should be considered in patients with risk of aspiration, even in absence of a foreign body or a history of aspiration.

OFP-12-014
KI67 index in malignant epithelioid mesothelioma
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Objective: Malignant mesothelioma is an aggressive, asbestos-related cancer with poor prognosis. Recently ki67 has been reported as an independent prognostic marker in malignant pleural mesothelioma or peritoneal epithelioid mesothelioma. This study examines retrospectively Ki67 in 39 consecutive malignant epithelioid mesothelioma (MEM) in order to evaluate the prognostic significance of this marker.
Method: Specimens from 31 consecutive MEM patients were assessed for Ki67 expression by immunohistochemistry. We used CONFIRM anti-Ki67 (Clone 30-9) rabbit monoclonal antibody on Ventana Benchmark platform. A pathologist scored Ki67 expression in the hottest spot and classified samples into 2 groups on the basis of expression (<25 % = low expression 18 cases (58.1 %); and ≥25 % = high expression in 13 cases (41.9 %)). Eight doubtful cases were scored by ImmunoRatio - JPEG2000 Virtual Slide microscope. Statistical analysis was assessed by SPSS 20.0.
Results: Median patient age was 66 years, 64.5 % were male patients. Tumour location was 87.1 % pleural and 12.9 % peritoneal. The median percentage of Ki67-positive tumour cells was 20 % (range: 1-80 %). There was no significant difference in the distribution with regard to age, gender, location or histology. Survival by Ki67 index were not statistical significance for low expression vs. high expression (mean 28.89 vs. 16.62 months) (Kaplan-Meier LogRank $p = 0.604$). Mean survivals by gender and were similar (male 22.4 vs female 26.18 months).
Conclusion: Ki67 evaluation is difficult and may not help to predict prognosis in MEM patients. Further studies are needed.

OFP-12-015
Incidence of therapeutic targets PD-L1 and EGFR1 in epithelial neoplasias of the thymus
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Objective: Objective:Targeted therapy of thymic epithelial tumours (TETs) following surgery can be considered in locally aggressive or metastatic tumours. Our aim was to evaluate PD-L1 expression and relevant mutations of the EGFR pathway in thymic epithelial tumours.
Method: Materials and methods: 37 TETs (29 thymomas and 8 thymic carcinomas) from a 10 years interval were analyzed by PD-L1 (clone SP142, Roche) and EGFR1 by immunohistochemistry. Further, EGFR1 exon 19 and 21, KRAS exon 2, BRAF exon 15 mutation status was determined following DNA direct sequencing.
Results: Results: Evaluation of PD-L1 expression in tumour cell showed a good reproducibility (inter-rater agreement, kappa-value: 0.840; Spearman $r = 0.966$, $p < 0.0001$). In 75 % of thymic carcinomas (6/8) and 68.96 % of thymomas (20/29) more than 1 % of tumour cells showed PD-L1 expression. The percentage of PD-L1 positivity was statistically not different (mean 21.87 vs. 39.82, respectively)($p = 0.5018$). EGFR protein expression was frequent (6/8), while none of the EGFR, KRAS and BRAF mutations could be detected.
Conclusion: Conclusions: PD-L1 and EGFR expression is common at variable levels in TETs suggesting a potential benefit of targeted treatments including the novel anti-PD-1/PD-L1 approach in aggressive cases. PD-L1 evaluation criteria can be applied in thymic epithelial tumours.

Wednesday, 6 September 2017, 14:00–16:00, Elicium 1
OFP-13 Molecular Pathology

OFP-13-001
EGFR T790M detection in plasma: Results from the Belgian ring trial
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Objective: Half of EGFR-mutated lung cancer patients treated with anti-EGFR TKI develop EGFR T790M-mediated resistance, resulting in disease progression. The availability of T790M targeting TKI and the possible unfeasibility of repeated biopsy testing indicate the need for sensitive T790M detection in plasma.
Method: No clinical samples were used due to ethical reasons. All samples were generated using cell line-derived sheared DNA, qualified by digital droplet PCR in quadruple. Based on current literature, we first defined the variant frequency and copy number range we aimed to test. Nine samples containing each 2 ml of spiked plasma were dispatched to the participating labs, making a total of eighty one samples.
Results: Three participants used the Cobas EGFR workflow, five used a digital droplet PCR (ddPCR) platform and one used a lab-developed NGS test. The first appears robust and reproducible to the 1 % level. The lab-developed NGS test was not able to detect the T790M mutation at the 1 % level and even 5 % level. The different ddPCR workflows showed different performances with two participants able to detect at the 0.05 % level. However, one ddPCR user also reported a 0.05 % L858R clone as T790M positive.
Conclusion: The Cobas workflow appears to have the advantage of being easy to use and interpret. But this assay is expensive per sample. The ddPCR workflows seems to have great potential but the challenging interpretation appears to be the major hurdle. The NGS test might have the advantage of being a comprehensive analysis but seems technically the most challenging for adequate implementation in the clinical lab.

OFP-13-002
Novel biomarker signature predicts sensitivity to PP2A activators in triple negative breast cancer
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Objective: Triple negative breast cancer (TNBC) patients derive little benefit from target-specific therapies due to lack of favourable prognostic targets. The aim of this project was to define biomarkers to measure PP2A complex deregulation in breast cancer, predicting a novel therapeutic class.
Method: Candidate PP2A activity biomarkers (PABs) were derived from in silico analysis of RNASeqV2 data from a breast cancer cohort ($n = 982$), retrieved from The Cancer Genome Atlas. PABs were validated in breast cancer cellular models. The Quantigene multiplex RNA assay was used to measure expression of these markers in a cohort of laser microdissected breast cancer ($N = 97$) and normal breast tissue ($N = 30$).
Results: Overexpression of these biomarkers predicts sensitivity to PP2A activator, FTY720, and are downregulated in a dose-dependent manner. PABs showed a lower expression in normal breast tissue compared to

matched tumour ($P < 0.004$). 37 % of TNBC cases express high levels of PABs comparable with the expression levels of FTY720-sensitive cell line models, and associated with negative prognostic indicators ($P = 0.023$).
Conclusion: TNBC cell lines sensitive to FTY720 show high expression of PABs. Using patient material, the PAB overexpression is common in the TNBC subtype. The novel biomarkers (PABs) provide a multiplex gene expression signature for a potential therapeutic group, sensitive to PP2A activators.

OFP-13-003
Designing a diagnostic FGFR3-TACC3 translocation assay using RT-PCR for glioblastoma multiforme patients
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Objective: The FGFR3-TACC3 fusion protein is a recurrent translocation in glioma patients and other types of solid malignancies, and is hypothesized to confer oncogenic transformation. Preliminary evidence of FGFR tyrosine kinase inhibitor (TKI) therapy has shown significant effectivity in vitro, in vivo and in phase I clinical trials, validating FGFR as a potential therapeutic target. A screening assay for the FGFR3-TACC3 translocation can thus be of great value for GBM patients, a patient population that currently lacks effective therapeutic interventions.
Method: A RT-PCR assay was designed to detect FGFR3-TACC3 fusion gene transcripts in FFPE tissue of archival GBM samples. FGFR3 immunostaining preselection was performed to identify potential FGFR3-TACC3 positive gliomas.
Results: Out of 467 gliomas, 14 (of which13 GBM) samples showed FGFR3 overexpression by IHC. Of these 14 FGFR3 positive samples, 8 fresh frozen samples were subjected to RT-PCR, revealing 5 FGFR3-TACC3 positive cases of the two most frequently occurring FGFR3-TACC3 fusion variants. Of these 5 cases, RT-PCR on FFPE material was performed, confirming the FGFR3-TACC3 translocation.
Conclusion: In conclusion, this study is the first to validate a FFPE tissue based RT-PCR screening method for the FGFR3-TACC3 translocation, thereby contributing to personalized cancer treatment of glioma patients.

OFP-13-004
One year experience of MET gene exon 14 skipping analysis in lung cancer: Identification of 18 cases by NGS
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Objective: Treatment of lung adenocarcinoma (LAC) is largely based on molecular characteristics of the tumour. Mutations in EGFR, HER2 and BRAF, specific translocations of ALK, ROS1, RET and amplification of MET all have diagnostic importance and lead to specific treatment options for the individual LAC patients. Recently, in 2–4 % of LAC MET gene mutations leading to skipping of exon 14 were found. LAC with MET exon 14 skipping mutations showed impressive responses to MET tyrosine kinase inhibitors (TKI) crizotinib, cabozantinib and capmatinib. We will present our experience with routine molecular diagnostic detection of MET exon 14 skipping mutations.
Method: In January 2016 we included in our routine molecular diagnostic NGS analyses 4 amplicons for detection of MET skipping mutations. The analyses were performed on DNA isolated from microdissected FFPE tissue sections or routine histology or cytology stained preparations. Nine different mutations were validated for their effect on splicing by RT-PCR.
Results: Between January 2016 and January 2017, 676 routine molecular diagnostic NGS analyses on LAC were performed. In 18 (2.7 %) cases MET mutations were detected. Nine out of 16 different mutations were tested by RT-PCR and all 9 were demonstrated to result in MET exon 14 skipping.
Conclusion: MET exon 14 skipping mutations can reliably be detected in routine pathology tissue samples by NGS. Confirmation of the mutational effect on RNA splicing can be implemented as well. Routine identification of MET skipping mutations (2.7 % of cases) adds substantially to the personalized targeted treatment strategies for LAC patients.

OFP-13-005
Systems-wide analysis of a CTCF haploinsufficiency model reveals dysregulation of cancer pathways
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Objective: CTCF is a highly conserved DNA-binding protein that acts as a master regulator of chromatin organisation and transcriptional regulation. CTCF is mutated in many human malignancies and is implicated as a tumour suppressor gene. Although mouse models of Ctcf haploinsufficiency are susceptible to spontaneous multi-lineage malignancies, the mechanism by which this occurs remains elusive. The objective of this study was to establish how a reduced genomic concentration of Ctcf increases susceptibility to cancer.
Method: We generated Ctcf heterozygous and homozygous mouse embryonic fibroblast cultures and applied chromatin immunoprecipitation followed by high-throughput sequencing (ChIP-seq), RNA sequencing (RNA-seq), proteomics, and chromosome conformation capture (HiC) to decipher potential tumour suppressor mechanisms.
Results: Transcriptome profiling identified hundreds of differentially expressed genes that were highly correlated with their corresponding proteins measured by tandem-mass tag proteomics (Spearman's rho = 0.65). Promoter marks measured by H3K4me3 ChIP-seq also showed significant overlap with altered gene expression. Gene set enrichment/pathway analyses showed significant enrichment for cancer pathways.
Conclusion: Multi-dimensional epigenome profile integration of this Ctcf haploinsufficiency model reveals that, despite chromatin stability, the modest transcriptional changes observed are in cancer pathways and might therefore explain how CTCF acts as a tumour suppressor.

OFP-13-006
TP53 protein expression rather than mutational status is predictive for survival in oesophageal adenocarcinoma
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Objective: TP53 mutations are frequent in esophageal adenocarcinoma (EAC) and proposed to arise early in EAC development. The role of TP53 as prognostic marker in EAC has not been established. This study aims evaluate the effect of TP53 on survival in treatment-naïve patients with surgically resected EAC.
Method: 216 patients with advanced EAC treated with esophagectomy alone were included. TP53 was evaluated by immunohistochemistry (IHC) on resection specimens and pattern of expression (overexpression (OE), normal expression (NE) and loss of expression (LOE)) was correlated with the disease free survival (DFS) using multivariable Cox regression analysis. In addition, 34 EAC were subjected to next generation sequencing of the entire TP53 gene.
Results: LOE and OE of TP53 as detected by IHC were independently predictive for adverse DSF in multivariable analysis, compared to NE

(LOE: HR = 2.754, 95%CI 1.547-4.903; OE: HR = 2.605, 95%CI 1.571-4.320, p-value:0.001). Mutations in TP53 detected in EAC correlated with IHC categories. Splice site-, frameshift or stop gain mutations were detected in EAC with LOE, while tumours with OE of TP53 showed non-synonymous single nucleotide variants.
Conclusion: TP53 LOE and OE behave similar compared to NE, and is an independent prognostic factor for DFS in patients with CRT-naïve EAC, correlating with mutational type of TP53.

OFP-13-007
Effect of mesenchymal stem cells, tumour infiltrating lymphocytes and cancer stem cells in the neuroblastoma
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Objective: Neuroblastoma (NBL) is the most common extra-cranial solid tumour in childhood. Cancer stem cells(CSCs) are thought to play a central role in tumour initiation, progression and recurrence. Increased levels of CSCs are associated with poor prognosis. The aim of this study is to investigate the interaction between neuroblastoma cells, CSCs and the elements of tumour microenvironment which is tumour infiltrating lymphocytes(TILs) and mesenchymal stem cells(MSC) ex vivo for the first time.
Method: Isolated fresh tissues of neuroblastoma surgical material were perfomed single-cell suspension and cultured. CD133+ stem cells were isolated using magnetic isolation from cultured neuroblastoma cancer cells. TILs were isolated by AIMV medium migration method MSC were isolated with CD54 +, CD90 + magnetic isolation. The isolated cells, tumour infiltrating lymphocytes and cisplatin were seeded in multi-well Plates Then the viability of cells measured at 24 and 48 hrs. Also phenotype of TILs were identified by flow cytometry and immunohistochemistry. Mann Whitney U testi test was used for the comparison of the nonparametric outcomes.
Results: A total of 20 neuroblastoma samples from patients who are 2 to 168 (mean 39) months old, were evaluated with cell culture. Half of them were at low risk group and the other half were at medium or high-risk groups. Ten females and ten males were included the study. It was observed that TILs and MSCs together protect neuroblastoma cells from the effect of cisplatin. TILs alone had no effect on CSCs; however MSCs protected CSCs from the effect of cisplatin.
Conclusion: This study showed that microenvironment favors the tumour by MSCs protecting CSCs from cytotoxic effects of cisplatin and TILs protecting both neuroblastoma cells and CSCs. Proving this interaction offers useful information to consider microenvironment in planning neuroblastoma and CSC-targeted therapies.

OFP-13-008
Systematic bias in genomic classification of breast cancer
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Objective: To compare tumour characteristics and treatment outcome between patients for which gene expression (GE) profiling was possible versus patients for which GE profiling was not possible, due to low tumour percentage or a low quality of the available tissue material.
Method: For this comparison a cohort of 738 patients who received neoadjuvant chemotherapy at the Netherlands Cancer Institute was used to determine a GE profile for research purposes. Validation was performed in a cohort of 812 patients treated with primary surgery.
Results: GE profiling could be performed in 53 % of the samples of the neo-adjuvant population. Patients with successful tumour gene expression profiling more often had high grade tumours (OR 2.56 (95%CI 1.77–3.71), $p < 0.001$) and were more often lymph node positive (OR 1.53 (95%CI 1.05–2.23), $p = 0.027$) compared to the group for which gene expression profiling failed. The association with grade was confirmed in the validation cohort.
Conclusion: Patients with successful GE profiling had a relatively more aggressive tumour phenotype than patients for which GE failed. It is important to acknowledge this bias in applying GE based tests on different patient populations than a test was developed on.

OFP-13-009
A next-generation sequencing assay to estimate tumour mutation burden from FFPE research samples
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Objective: High tumour mutation burden is a biomarker shown in some cancer types to predict positive response to immune checkpoint inhibitors. We utilize a targeted cancer research panel to estimate tumour mutation burden.
Method: We present a single sample analysis workflow for estimating tumour mutation burden from FFPE research samples. Our assay utilizes a PCR-based target enrichment panel that covers ~1.7 Mb of total genomic space. Our customized workflow requires only 20 ng of input DNA and enables a 2 day turn-around time from sample to the final report. The workflow enables < 60 min of hands-on time for automated library preparation and templating on a batch of 8 samples. Sequencing is performed on high throughput semiconductor sequencing platform to achieve sufficient depth (~500× coverage) and accuracy. Our analysis pipeline calls somatic variants on the tumour sample only, with no matched normal sample, and applies filters to remove germ-line variants.
Results: Through in silico analysis performed on The Cancer Genome Atlas (TCGA) data we show that the panel can achieve > 90 % sensitivity and > 95 % specificity to distinguish high and low mutation burden samples. Our filters consistently eliminate ~98 % of germ-line variants from the set of all variants called in a single sample analysis workflow. Evidence from tumour-normal analyses on matched tumour and normal samples suggests that our single sample analysis, on the tumour sample only, detects somatic mutations with high sensitivity and specificity.
Conclusion: A simple workflow has been developed on the Ion Torrent sequencing platform to estimate per megabase somatic mutational burden. This solution can help advance research in immuno-oncology.

OFP-13-010
Sensitive and specific variant detection in circulating tumour DNA by anchored multiplex PCR and NGS
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Objective: Liquid biopsies are a promising, minimally invasive alternative to tissue biopsies that may have a greater ability to interrogate heterogeneous tumours. However, circulating tumour DNA (ctDNA) is highly fragmented and is usually of low abundance. Therefore, NGS-based assays to detect variants in ctDNA must be sensitive enough to detect mutations at low allele frequencies (<2 %) from <100 ng of highly fragmented DNA. We developed a targeted NGS assay based on Anchored Multiplex PCR (AMP™) for sensitive and specific detection of mutations in liquid biopsy-derived ctDNA.
Method: AMP uses unidirectional gene-specific primers and molecular barcoded adapters (MBC) for amplification, enabling enrichment of small ctDNA fragments from a single primer-binding site. MBC adapters

permit post-sequencing error correction, reducing background noise and increasing analytical sensitivity.
Results: This assay demonstrates 100 % detection sensitivity for 1 % AF variants using 10 ng DNA input and 71.9 % detection sensitivity for 0.1 % AF variants using 50 ng DNA input. Post-sequencing error correction with MBC adapters results in 91.7 % specificity. Finally, mutations detected from liquid biopsy-derived ctDNA show cancer type-dependent concordance with tissue biopsy findings, and reveal additional oncogenic driver mutations.
Conclusion: These results indicate that AMP-based NGS is a powerful tool for sensitive and specific NGS-based detection of variants in liquid biopsies.

OFP-13-011
Characterisation of B- and T-cell immune repertoires using anchored multiplex PCR and next-generation sequencing
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Objective: The immune repertoire (IR) provides a means to monitor adaptive immune responses to disease, vaccination and therapeutic interventions. NGS-based IR characterization usually requires large primer panels to capture its extensive combinatorial diversity and a complex system of synthetic controls to account for differential amplification efficiency across segment combinations. Here, we describe an Anchored Multiplex PCR (AMP™)-based NGS assay to analyze the IR, employing a minimal set of gene-specific primers in conjunction with molecular barcodes (MBCs) to reduce amplification bias.
Method: AMP is a library preparation method for NGS that uses MBC adapters and gene-specific primers for amplification, enabling immune chain mRNA interrogation from a single side. This eliminates the need for opposing primers that bind within the highly variable V-segment and facilitates CDR3 sequence capture from highly fragmented RNA inputs.
Results: This assay demonstrates high reproducibility between replicates and quantitative clone tracking down to 0.01 %, with the ability to determine IGHV mutational status. Our data indicate that clonal diversity in sequencing data is primarily driven by input quantity and total T-cell number.
Conclusion: AMP-based NGS with MBC quantification and error-correction is a powerful method to characterize the immune repertoire.

OFP-13-012
Evaluating overlap of circulating and tumour-infiltrating T-cells using AmpliSeq-based Ion Torrent TCRB immune repertoire sequencing
T. Looney*, E. Linch, L. Miller, D. Topacio-Hall, L. Lin, A. Pankov, J. Zheng, K. Bergefall, A. Mongan, G. Lowman, F. Hyland
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Objective: TCRβ immune repertoire analysis by next-generation sequencing is emerging as a valuable tool for research studies of the tumour microenvironment and potential immune responses to cancer immunotherapy. Here we describe a multiplex PCR-based TCRβ sequencing assay that takes advantage of the exceptionally low base-call error rate and long read capability of the Ion S5 530 chip.
Method: We evaluated assay performance by 1) sequencing TCRβ rearrangements from donor peripheral blood leukocyte (PBL) cDNA that had been spiked with 30 reference rearrangements taken from literature and 2) deeply sequencing libraries prepared from 10 ng to 1 ug of PBL cDNA. We then evaluated the extent of clonal overlap between matched tumour infiltrating lymphocyte (TIL) and peripheral blood leukocyte repertoires in an individual with squamous cell carcinoma of lung.
Results: Results from sequencing of spike-in reference rearrangements indicate that the assay is accurate and sensitive over 5 logs of input template amount while showing minimal amplification bias. Rarefaction analysis of deeply sequenced libraries revealed libraries prepared from <100 ng PBL template to approach saturation at <15 M reads depth. Sequencing of matched PBL and TIL repertoires showed that a subset of the PBL repertoire (8 %) consisted of clones also found in TIL. Technical replicates showed high concordance (r > .96) in the frequency of detected clones, indicating that the results were reproducible and samples were sequenced to an appropriate depth.
Conclusion: In summary, these data suggest that AmpliSeq-based multiplex PCR and Ion Torrent sequencing provide unbiased, reproducible, scalable, complete, and accurate information for immune repertoire research sequencing applications.

Wednesday, 6 September 2017, 14:00–16:00, G104-105
OFP-14 Joint Session: History of Pathology / Haematopathology

OFP-14-001
Restoration of 50+ year old pathology museum specimens from the University of Papua New Guinea (UPNG)
R. Cooke*
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Objective: This poster demonstrates how a 50 year old teaching pathology museum in a poor country, Papua New Guinea is being rejuvenated so that it can continue to be used for teaching. Similar advice was given to the Curator of the museum in the University of Indonesia. This Museum consists of specimens that were mounted before 1940. The Curator has managed to remount most of the old specimens in newly, custom made perspex display cases.
Method: Pathology museums in many more affluent countries have been neglected, but there is now a resurgence in interest in teaching pathology to doctors and other health professionals. These museum specimens are irreplaceable and they need to be rejuvenated so that they can be used again for teaching.
Results: This poster illustrates how it was done in PNG with seed funding from the Royal Australasian College of Surgeons. The remounting process has continued during the 18 months since it was started. New display cases have been purchased and the Curator has added photographs of the specimen descriptions that allow students to study at their leisure.
Conclusion: The PNG collection contains examples of Tropical Diseases that occurred in the stone age population at the time of first contact with Western Medicine. These are important historical records. Photographs of clinical cases from that era, and photographs of the microscopic appearances are being added to the display of potted specimens to further enhance the teaching value of the museum specimens.

OFP-14-002
Quain's fatty heart
R. Henriques de Gouveia*, T. Ferreira, M. J. Aguiar, A. Lopes, L. Carvalho, F. Corte Real
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Objective: Obesity, visceral/epicardial fat, heart steatosis and their influence in cardiovascular disease are under international scientific investigation spotlights. Yet, this issue's concern goes back for centuries, namely to the Irish physician Sir Richard Quain, whose surname was used to coin a cor adiposum synonymous. The authors intend to know the old and the new about 'fatty heart'.

Method: 1)Sir Richard Quain's life/career/publications were explored. 2)Heart Specimens from UNESCO's World Heritage 'Faculty of Medicine Pathology Museum of Coimbra's University' were examined. 3)Forensic Institute daily practice Heart Specimens were also gross and microscopically examined.
Results: Sir Richard Quain (1816–1898), born at Mallow-on-the-Blackwater, was a brilliant student and an outstanding physician, dying in London (aged 81). One of his renowned works/publications was on "fatty heart". His findings will be exemplified/completed by our own data, both from Pathology Museum's 100 year-old cardiac specimens and from actual heart specimens.
Conclusion: The study of normal and pathological heart adipose tissue is crucial from physiopathological, therapeutic and medico-legal points of view. Studies in old XIXth Museum specimens give information about cardiac pathology back then, allow new investigations and comparison with recent specimens. Quain's Fatty Heart is a bridge between old and new knowledge on cardiovascular pathology.

OFP-14-003
Medical Museums in Europe beginning in the Renaissance
R. Cooke*
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Objective: To demonstrate exhibits in European Medical Museums starting in Padova and Florence and then moving to Paris, London, Edinburgh, Vienna, Berlin, Moscow, Spain, Portugal, Lyon, Pavia, Leiden, Amsterdam
Method: The talk will be illustrated by photographs taken by the author with the permission and assistance of Curators of the various Museums.
Results: The Cooke's Tour of the Museums demonstrates the development of Medical thought over the past 500 years and emphasises that the practitioners of modern medicine are standing on the shoulders of their predecessors.
Conclusion: Some of these historical museums have passed through periods of neglect, but in many countries their importance is being recognised by the fact that Governments are currently spending money on refurbishing them.

OFP-14-004
ABC Subfamily C Member 10 (ABCC10) is a promising novel target in Hodgkin's lymphoma
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Objective: The aim of this study was to determine the expression level of ABCC10 in HL cells and its potential prognostic/predictive significance. We also aimed to investigate ABCC10 reverasal effect on HL cells chemosensetization.
Method: Gene expression data set analysis to investigate mRNA expression of ABCC10 in an already published data set. Western Blot was used to delineate the protein level of ABCC10 in HL cell lines, Quantitative real-time PCR was conducted to determine the mRNA expression level of the target gene in both tumour cells and normal lymphocytes. We determined the effect of ABCC10 reverasal by its inhibitor Tariquidar" and its chemosensitization effect on HL cells by applying in-vitro proliferation assay. Immunohistochemistry was performed on HL paraffin sections to evaluate the expression of ABCC10 on primary HL tumour.
Results: Results of our study showed that ABCC10 is expressed in HL derived cell lines and primary HL tumour cells. Our functional studies showed that inhibition of ABCC10 by one of its inhibitor (Tariquidar) had a significant dose-dependent increase in the sensitivity of HL cells to doxorubicin. In our study we also found that overexpression of ABCC10 was considered to be a negative prognostic factor for HL patients.Moreover, we found that ABCC10 expression can affect HL patients' outcome.
Conclusion: These results indicate for the first time that ABCC10 plays a role in increasing toxicity of chemotherapy on HL cells, its overexpression affect clinical outcome, and it is a potential target in HL.

OFP-14-005
Over-expession of Thioredoxin-1 affects tumour growth and is a promising target in Hodgkin's lymphoma
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Objective: The aim of this study was to determine the expression level of Thioredoxin-1 (TRX-1) in HL cells and its potential prognostic/predictive significance in HL. Also to investigate the effect of targeting TRX-1
Method: Western Blott, IF & IHC was used to investigate the protein expression level of TRX-1 in HL cell lines and tumour tissues, Quantitative real-time PCR to determine the TRX-1 mRNA level. TRX-1 knock-down was done using siRNA. PX-12 was used to reverse TRX-1 effect.
Results: Results of our study showed that TRX-1 is over-expressed in HL cell lines and primary HL tumour cells while it is expressed in a lower level in normal B cells. We showed that TRX-1 knock-down had a significant reduction effect on HL cell lines proliferation. Moreover, we showed that HL cells are sensitive to one of TRX-1 inhibitor, PX-12 which significantly reduced HL cells proliferation in a dose-dependent manner. In our study we also found that TRX-1 is expressed in all cHL cases with variable intensities, and considered as a negative prognostic factor.
Conclusion: Overexpression of TRX-1 plays a role in increasing survival of HL cells, affect HL patient's clinical outcome, and it is a potential novel target in HL.

OFP-14-006
Translation initiation factors as novel prognostic biomarkers of aggressive B-cell lymphomas
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Objective: Eukaryotic translation initiation factors (eIFs) are crucial participants in the first steps of eukaryotic protein synthesis and their dysregulation has been implicated in cancerogenesis. Since there is only limited data on the role of eIFs in diffuse large B-cell lymphoma (DLBCL), we aimed to comprehensively study eIFs in this type of aggressive lymphomas.
Method: By using a publically available gene expression data set of DLBCL patients, we correlated eIF expression with cancer specific survival. Additionally, lymphoma patient specimens were tested for eIF expression, primary DLBCL tissue samples were immunohistochemically analyzed (4 eIFs in 30 patients). Expression of 15 eIFs was investigated in 6 DLBCL and 2 Burkitt lymphoma (BL) cell lines and compared to expression in an immortalized B-cell line by Western blotting.
Results: In DLBCL, 7 out of 54 tested eIFs are significantly associated with shorter, cancer specific survival ($p < 0.05$). Immunohistochemistry further indicated subtype-specific expression differences for 3 out of 4 tested eIFs in DLBCL. In DLBCL and BL cell lines, eIFs are higher expressed than in the immortalized B-cell line.
Conclusion: Our study implicates a role for eIFs in lymphoma development representing a basis for further evaluation of eIFs as potential biomarkers and/or therapeutic targets in aggressive B-cell lymphomas.

OFP-14-007

Developing a multiplex next-generation sequencing assay to study highly clonal tumour samples

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Objective: To demonstrate a research use only workflow that includes library preparation, sequencing, and data analysis to enable high molecular capturing efficiency and detection of ultra-low frequency DNA variants in blood samples. Such workflow brings promises to accelerate clinical trials by improving prognosis and develop better insights into evolution of highly clonal tumours, like AML. Such tumours are composed of multiple related subclones that are invisible to conventional diagnostic methods, yet they commonly represent a significant clone at the time of relapse.
Method: We present computational methods used in assay development, followed by an analysis algorithm that models errors accumulated during amplification and sequencing to enable sensitive and specific detection of somatic mutations down to the frequency of one in hundred thousand. We used our design methods to develop a next generation sequencing assay that allows interrogation of ~360 biomarkers relevant to multiple tumour types from COSMIC and Oncomine™ databases.
Results: We demonstrate assay performance and accuracy of variant analysis in human contrived control samples. The assay delivers >95 % on target reads and highly uniform amplification across targeted DNA molecules with input DNA of 1 ng or higher, and has a fast turnaround time from extracted DNA to variants of less than 28 hr. Across multiple input DNA amounts we observed high molecular capturing efficiency of higher than 50 %. For inputs of 10, 100, and 1000 ng, corresponding to, 6 K, 60 K, 600 K single stranded genomic copies, our assay detected more than 3, 30 and 300 K copies.
Conclusion: We demonstrated highly sensitive and specific workflow that may facilitate researchers to study samples with high molecular diversity and detect biomarkers present at 1:100,000 allele frequency.

OFP-14-008

Neutrophil and monocyte CD64 and HLA-DR expression evaluation in SIRS by flow cytometry

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Objective: Determine the expression of CD64 and HLA-DR on neutrophils and monocytes by flow cytometry
Method: Study was conducted on the samples of peripheral blood of 28 oncological patients by using the flow cytometer Navios (Beckman Coulter, USA).
Results: It was established that the value of RFI (relative fluorescence intensity) (the expression ratio of CD64 between neutrophils and monocytes) varied within the range of 0,1–0,7. RFI of CD64 was 0,07–0,16 in the patients without the systemic inflammatory response (SIRS). The average RFI of CD64 value was 0,14. RFI value of CD64 ranged from 0,17 to 0,59 in all cases with SIRS. The average RFI value of CD64 for SIRS was 0,43. Besides, the expression of the CD14 + HLA-DR– cell population varied from 8,0 to 19,1 % in patients without SIRS, while this value was within the range of 67,0–89,9 % in patients with SIRS.
Conclusion: Thus, high RFI values of CD64 and activation markers on the CD14 + HLA-DR– population correspond to the presence of SIRS. Thus neutrophil expression levels of CD64 and CD14 + HLA-DR–can be used as the parameter for SIRS, which has a potential role in therapeutic monitoring.

OFP-14-009

Genetic profiling and mutational analysis of myeloproliferative neoplasms using next generation sequencing

S. Jain*, S. Gajendra, R. Sharma, S. Mehra, N. Sood, R. Sachdev
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Objective: The study aimed to identify new mutations in Myeloproliferative Neoplasms(MPNs)using Next Generation Sequencing(NGS) which may be diagnostic and help determine prognosis.
Method: Seventy cases of BCR-ABL1 negative MPNs were evaluated over 1.5 years. Molecular Profiling was done(ION Torrent PGM) using a 50 gene panel.
Results: Molecular profiling showed JAK2 was the commonest mutation seen in Polycythaemia Vera(PV,100 %),Essential Thrombocythaemia(ET,73 %) and Primary Myelofibrosis (PMF,52 %). Mutations like KIT, TP53, APC, CTNNB1, STK11 were found to be statistically significant. Analysis of individual MPNs revealed APC and HRAS mutations in JAK2 negative ET and PDGFRA in JAK2 negative PMF. The haematological parameters studied showed JAK2 positive patients had a higher mean age, haemoglobin, total leucocyte count and platelet count. JAK2 mutation was found to be associated with intermediate and high risk ET. Mutations like TP53,APC and CTNNB1 were seen predominantly in intermediate and high risk groups.
Conclusion: The identification of new mutations will help not only in diagnosis but also for better understanding of clinical behavior of MPNs. It will help identify subset of high risk patients to be kept under strict follow up and also develop new targeted therapies. This is the first study of its kind in the Indian subcontinent, to the best of our knowledge.

OFP-14-010

Possible DNA demethylation effect on de novo DNA methyltransferase expressions in cell line derived from multiple myeloma

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Objective: DNA methyltransferases (DNMTs) including DNMT1, DNMT3a and DNMT3b, catalyze the transfer of methyl groups to cytosine position 5, and play an important role in epigenetic regulation, which could be involved in pathogenesis of multiple myeloma (MM) or monoclonal gammapathy of undetermined significance (MGUS). DNA demethylation is necessary for the epigenetic reprograming of genes and is directly involved in tumour progression. Passive DNA demethylation usually takes place on newly synthesized DNA strands via DNMT1 during replication rounds. Active DNA demethylation occurs during 5-methylcytosine through TET (Ten Eleven Translocation) enzyme-mediated oxidation removal, and this process can be repaired directly by conversion of cytosine via de novo DNA methyltransferases, DNMT3a and DNMT3b.
Method: The expression of DNA methyltransferase was analysed by RT-PCR in CCL-155 (RPMI-8226) human multiple myeloma cells treated with two types of inhibitor of the DNMTs (5-azacytidine and disulfiram) and one type of histone deacetylase inhibitor (suberic bishydroxamata, SBHA). The impact on gene demethylation and global DNA methylation status were colorimetric assessed.
Results: The expression of DNMT3a in multiple myeloma cells after treatment with disulfiram increased while DNMT1 expression was not changed. Similarly, the cell treatment with 5-azacytidine induced the increase of DNMT3b expression but the expression of DNMT1 was not influenced.
Conclusion: Multiple myeloma cells treated with inhibitors of DNMTs exhibited increased expressions of de novo DNA methyltransferases DNMT3a and DNMT3b. We deduce that this process could explain the onset of demethylation treatment failure in multiple myeloma cells. This study was supported by grants LF_2017_021 and NPS I LO1304 from the Czech Ministry of Education.

OFP-14-011

Purification of Hodgkin and Reed-Sternberg cells from FFPE tissue sections using the DEPArray

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Objective: Classic Hodgkin's lymphoma (cHL) is characterized by the presence of CD30-positive and morphologically distinct—often multinucleated—tumour cells, the so-called Hodgkin (H) and Reed Sternberg (RS) cells. A unique feature of cHL is the low tumour cellularity, comprising up to 5 % of all cells. In the present work we demonstrate the purification of HRS cells from FFPE tissue sections using the DEPArray™ technology.
Method: FFPE tissue sections were disaggregated to a single cell suspension and stained for CD30 (BerH2) and DAPI. By DEPArrayTM technology, CD30-positive HRS cells were selected and morphologically evaluated. Then, pools of HRS cells and lymphocytes were recovered consecutively and whole genome amplified. Ultimately Ampli1™ LowPass sequencing kit was used to assess genome-wide copy-number aberrations (CNA).
Results: CNA profiles enabled a distinct discrimination of malignant HRS cells from non-malignant lymphocytes: HRS cells exhibited an aberrant CNA profile with multiple gains and losses, while lymphocyte pools showed a generally flat profile.
Conclusion: The automated, image-based DEPArray™ sorting technology enables the precise selection and isolation of rare HRS cells from FFPE cHL-derived samples as demonstrated by the aberrant CNA profiles of the purified HRS cells.

OFP-14-012
Type-I Interferon signature in cutaneous blastic plasmacytoid dendritic cell neoplasm
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Objective: Expression of type I Interferon (IFN-I)-induced genes in cutaneous Blastic Plasmacytoid Dendritic Cell Neoplasm (cBPDCN).
Method: Skin biopsies of 19 cBPDCN, 5 acute myeloid leukemia (cAML), 28 Lupus Erythematosus (cLE) and 7 normal skin (NS) were used. Immunohistochemistry (IHC) for MXA and phosphorilated STAT1 (p-STAT1) were performed on all samples. RNA was extracted from FFPE sections of 5 cBPDCN, 5 cAML, 4 cLE and 4 NS cases. qRT-PCR was performed for RSAD2, STAT1, SIGLEC1, IFIT1, MXA and IFI27 genes to calculate the Interferon Score (IFN-S)(Rice et al., 2013).
Results: All cLE showed diffuse expression of MXA and pSTAT1 on inflammatory infiltrate and keratinocytes. In 18/19 cBPDCN cases MXA was positive on tumour cells, while its expression in keratinocytes was observed in 6/18, similarly to pSTAT1. MXA and pSTAT1 were negative in cAML and NS. IFN-S was positive (186.137) in all cLE and negative (17.531) in cBPDCN. Interestingly, samples with MXA+ keratinocytes had higher expression of MXA, but not of other genes. Moreover, cAML did not express MXA, but RSAD2, STAT1, SIGLEC1 and IFI27 were higher than in cBPDCN.
Conclusion: Data on IFN-I production by BPDCN are conflicting. This study shows lack of IFN-S in this tumour and identifies a subgroup of cases with isolated high MXA expression.

Wednesday, 6 September 2017, 14:00–16:00, Emerald Room
OFP-15 Joint Session: Neuropathology / Ophthalmic Pathology

OFP-15-001
Lymphomatosis cerebri: A rare and under-recognised pattern of primary central nervous system lymphoma
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Objective: Primary central nervous system (CNS) lymphoma (PCNSL) is a diffuse large B-cell lymphoma (DLBCL) confined to the CNS in immunocompetent patients. PCNSL usually forms a mass; biopsy and histopathological confirmation are necessary for appropriate treatment. Rarely, PCNSL diffusely infiltrates the CNS, with no discrete mass ("lymphomatosis cerebri"). Coupled with corticosteroid effects in a biopsy, this presentation may cause diagnostic delay.
Method: A previously well 21-year-old female presented with progressively unsteady gait and seizures. Magnetic resonance imaging showed confluent white matter T2 / FLAIR hyperintensity involving the cerebral hemispheres, cerebellum and brainstem, consistent with an infective, inflammatory or demyelinating process. Following a clinical diagnosis of acute disseminated encephalomyelitis, methylprednisolone, intravenous immunoglobulin, plasmapheresis, and cyclophosphamide were administered without sustained improvement. A brain biopsy performed at an external institution 3 months after presentation showed gliosis and perivascular macrophage infiltrates.
Results: A second biopsy from the right cerebral hemisphere, performed in our centre after severe clinical deterioration in the subsequent 4 months, showed an infiltrative tumour consisting of large pleomorphic lymphoid cells with the immunoperoxidase staining profile of a DLBCL. The patient expired 6 weeks later.
Conclusion: Awareness of lymphomatosis cerebri, and that corticosteroids might compromise the diagnostic yield in a biopsy may aid more timely management.

OFP-15-002
Dual-genotype oligoastrocytoma: An underestimated entity?
V. Barresi*, S. Lionti, L. Valori, G. Gallina, M. Caffo, S. Rossi
*University of Messina, Dept. of Human Pathology, Italy

Objective: To describe a unique case of dual-genotype oligoastrocytoma with IDH2 mutation.
Method: The tumour was resected from the temporal lobe of a 25 year-old man. The whole surgical specimen was formalin fixed and paraffin embedded for histological examination with haematoxylin and eosin (H&E) stains and immunohistochemistry. IDH1 and IDH2 genes sequencing, Telomerase Reverse Transcriptase (TERT) promoter mutational analysis and 1/19q Fluorescent In Situ Hybridization (FISH) were performed separately in tumour fragments with different morphology and immuno-phenotype.
Results: Histological examination showed distinct oligodendroglial and astrocytic areas. The former retained alpha-thalassaemia/mental retardation X-linked (ATRX) immuno-expression and had absent staining for p53, while the latter had ATRX loss and p53 over-expression. Gene sequencing disclosed IDH2 mutation in both areas, while oligodendroglial, but not astrocytic areas, had 1p/19q codeletion and Telomerase Reverse Transcriptase (TERT) promoter mutation. Based on those finding,s low grade dual-genotype oligoastrocytoma was diagnosed.
Conclusion: Identification of dual-genotype oligoastrocytoma might be clinically relevant for prognosis and therapy. The incidence of this entity might be underestimated due to sampling biases or to the use of immunohistochemistry and molecular analyses in a limited portion of the tumour. We believe that further analyses on morphologically heterogeneous diffuse gliomas are warranted before dismissing oligoastrocytoma as a distinct nosological entity.

OFP-15-003
Rhabdoid meningioma: Grading and prognostic significance of this unusual histotype
V. Barresi*, M. Caffo
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Objective: To describe the histopathological features and clinical outcome of two rhabdoid meningiomas with no histological evidence of malignancy.

Method: Two rhabdoid meningiomas with no histological evidence of malignancy were found in our archive over a period of 20 years.
Results: One case was resected from a 73 year-old woman. The tumour was rhabdoid for its 75 % and had 2 mitoses per 10 high power fields (HPF), prominent nucleoli, foci of spontaneous necrosis, sheeting and small cells with high nuclear/cytoplasmic ratio. Ki-67 labeling index (LI) was 1 %. Based on the histological features, it was classified as WHO grade II. The patient had not recurrences and was alive at 114 months follow-up. The second case was resected from the frontal convexity in a 39 year-old woman. The neoplasia was rhabdoid for its 80 %. Mitotic index was 1/10HPF. Neoplastic cells had prominent nucleoli and sheet-like growth. Ki-67 LI was 4 %. The tumour was graded as WHO grade I. No recurrence was observed along 7 months follow-up.
Conclusion: These cases demonstrate recent evidence that rhabdoid morphology per se is not associated with aggressiveness of meningiomas and that rhabdoid meningioma should not be considered as WHO grade III in the absence of malignant features.

OFP-15-004
Eukaryotic initiation factors might not only represent novel targets for glioma therapies but might also monitor drug effectiveness
S. Krassnig*, A. Orthmann, A. M. Toeglhofer, C. Wohlrab, N. Golob-Schwarzl, C. Wodlej, M. Pennauer, A. Raicht, K. Mahdy Ali, G. von Campe, M. Gogg-Kamerer, M. Logi, S. Sygulla, J. Hoffmann, S. Weis, M. Benesch, J. Haybaeck
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Objective: Glioblastoma (GBM) represents the most common brain tumour in adults. The current outcome is still very poor. Translation initiation regulated by eukaryotic initiation factors (eIFs) is one rate limiting step of protein synthesis. Alterations of eIFs might lead to uncontrolled cell proliferation and promote gliomagenesis.
Method: Survival data were retrieved from "The Cancer Genome Atlas" database. Biochemically, eIF expression was analysed in human glioma samples on protein and mRNA level. Additionally, GBM mouse xenografts were treated with established agents and evaluated regarding their eIF expression profile.
Results: Survival analyses showed significantly improved overall survival in GBM patients with low tumour eIF4H levels. Basic characterisation of various eIF subunits in human cancer tissue revealed an up-regulation of eIF4H and additional eIFs on protein and mRNA level. In GBM mouse xenografts, temozolomide and regorafenib significantly down-regulated eIF protein-expression. This decrease could not be observed in temozolomide-resitant GBM models. Combination of temozolomide and other agents did not additionally affect eIF expression.
Conclusion: eIF levels are not only increased during gliomagenesis but also seem to reflect the treatment effectiveness. eIFs might therefore represent novel prognostic and predictive markers for GBM patients and their clinical outcome.

OFP-15-005
Predictors of long-term outcome in diffuse gliomas
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Objective: Recent studies suggest that current WHO grading criteria may fail to predict outcome of IDH-mutant diffuse gliomas. We aim to analyze a large cohort of diffuse gliomas (WHO grades II-III) in order to identify histological predictors of outcome stratified by molecular profile.
Method: A cohort of patients diagnosed with diffuse gliomas between 1990 and 2005 at a single center is being assessed for histological features as well as IDH, ATRX and 1p19q co-deletion status and overall survival.
Results: Patients with IDH-mutant gliomas ($n = 71$) were followed up for up to 26 years. Sixty-eight percent and 55 % of patients with IDH-mutant tumours were alive 10 and 20 years after diagnosis, respectively. Overall survival was lower for ATRX-deficient (median 9.0 years) than for ATRX-proficient tumours (median not reached). WHO grade did not predict overall survival.
Conclusion: This study confirms that WHO grade (according to current criteria) does not predict overall survival in IDH-mutant gliomas other than glioblastoma. Retrospective studies may be a valuable data source to assess very long-term outcome of IDH-mutant diffuse gliomas and to redefine grading criteria.

OFP-15-006
Parkinson's disease: Myenteric gliosis in an experimental rat model
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Objective: Parkinson's disease gastrointestinal disturbances frequently start during premotor phase. GI dysfunction in rats infused intranasally with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine(MPTP), may be a model for early premotor phase of PD.
Method: Male Wistar rats (16 weeks) ileum segments were collected 12 days following MPTP administration. Isometric contractile concentration-response curves for dopamine(DA) were performed in presence/absence of sulpiride (selective dopamine D2-like receptors(D2R) antagonist). Dopaminergic status was assessed by measuring total DA content(HPLC) and TH density (WB). S100β (enteroglial intestinal inflammation marker) glial fibrillary acidic protein (GFAP gliosis marker) and cellular location of D2R immunoexpression were validated/ FFPE tissue.
Results: Results: Functional studies showed MPTP statistically significant decrease in DA maximum contractile effect compared to saline group. Sulpiride significantly decreased the DA-induced maximum contraction in control group. No significant difference was obtained in MPTP group.
Conclusion: Results suggest that MPTP is perturbing D2R-dependent ileum function. D2R immunoreactivity was observed in ganglion cells of myenteric plexus. Dopaminergic dysfunction occurred with preserved DA homeostasis. MPTP group evidenced apparent increase in S100β and GFAP immunoreactivity lower expression in myenteric plexus compared to saline group. Expansion of intestinal villi lamina propria in MPTP group suggests early gut dopaminergic dysfunction underlined by myenteric gliosis and mucosal inflammation following MPTP administration.

OFP-15-007
Heterogeneous chromosomal profiles in a unique series of DIPG in children and young adults
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Objective: Diffuse intrinsic pontine gliomas (DIPG) are aggressive tumours with poor prognosis and no effective treatment. The identification of histone H3.3 mutations has been a large advance by defining groups with different prognoses. However, chromosomal alterations still need to be detailed and correlated with histological and clinical data in order to improve therapeutic strategies.
Method: We provide here a unique and large series of 53 DIPG cases with pre-treatment samples of the tumour for each patient.

A complete study of chromosomal alterations by CGH-array has been performed on FFPE and frozen samples. Immunochemistry and next-generation sequencing data are also available.
Results: CGH-array highlights sub-groups with heterogenous chromosomal profiles from no alteration to complex modifications. Histological grading doesn't seem to be correlated with these chromosomal alterations.
Conclusion: This complete study of chromosomal alterations in a large series of DIPG has never been performed before. Results are promising by showing original profiles, different from those observed in gliomas in adults. They will be correlated to survival data.

OFP-15-008
Solitary fibrous tumour: Clinicopathologic, STAT6 immunohistochemical analysis and reclassification according to recent WHO guidelines of 39 cases
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Objective: Solitary fibrous tumour (SFT) is an uncommon fibroblastic neoplasm. Molecular analyses have discovered that almost all SFTs harbour an NAB2-STAT6 fusion gene, being STAT6 immunohistochemistry a reliable surrogate of the fusion gene. Recent 2016 World Health Organization Classification of Tumours of the Central Nervous System restructured SFT and hemangiopericytoma as one entity and adapted a grading system to accommodate this change. We performed STAT6 in all cases diagnosed in our department and reclassified all meningeal cases.
Method: 39 cases of SFT were identified. Clinical information included treatment and patient outcome. Cellularity, mitotic index and necrosis were re-evaluated. STAT6 immunohistochemistry was done in freshly cut sections. Nuclear staining of >/=5 % of cells was deemed positive. Intensity and extent of staining were scored.
Results: Patients included 23 men and 16 women, with a median age of 56 years. Sixteen occurred in the meninges. Median follow-up time after surgery was 930 days. 35 SFTs showed nuclear expression of STAT6. The staining was diffuse in 20 cases and intensity was moderate/strong in 25 cases. Re-evaluation of tumours resulted in upgrading 4 cases to grade III.
Conclusion: STAT6 immunoreactivity can be diagnostically helpful when considering SFT, particularly in the meninges. Reclassification can be important for treatment and prognosis.

OFP-15-010
Chromosomal aberration predicts uveal melanoma mutation
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Objective: Uveal melanoma (UM) is the most frequent primary eye cancer in adults. Copy number variations (CNV), gene expression profiling, and the recurrent gene mutations in BAP1, SF3B1, or EIF1AX, can be used to stratify patients for risk of metastatic disease. This study aims to identify whether common chromosomal aberration patterns are related to UM gene mutation status and vice versa, whether the mutations correspond to a specific chromosomal signature in UM.
Method: SNP array data of 214 UM was available. Mutational status of the 5 core genes was determined in 209 tumours. Unsupervised hierarchical clustering of the array data resulted in five distinct clusters. Based on the mutational status the array data was analyzed for recurring CNV.
Results: BAP1-mutated (immunohistochemical-negative) tumours have the largest CNV in size (whole chromosome or chromosome arms). SF3B1-mutated tumours were characterized by multiple (>3) structural aberrations of the chromosomes. EIF1AX-mutated UM were characterized by a relative lack of UM specific CNV.
Conclusion: UM harbor mutation-specific chromosomal patterns. These patterns are characterized by different types of chromosomal anomalies, thus illustrating that distinct biological mechanisms underlie UM pathogenesis. These pathways could possibly be specifically targeted with future diagnostics and types of treatment.

OFP-15-011
Retrospective study of prognostic histopathological features and mutation status in conjunctival melanomas
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Objective: Metastatic conjunctival melanomas carry a grim prognosis. This emphasizes the need for early detection of aggressive lesions. In this study we focus on the relationship between histopathological parameters, mutation status and outcome.
Method: We selected patients diagnosed at the Pathology Department of the Erasmus Medical Center (EMC) and treated in both the EMC and the Eye Hospital in Rotterdam, the Netherlands, from 1987 until 2017. Histopathological sections of the primary lesions were reviewed for various histopathological parameters. Furthermore the telomerase reverse transcriptase (TERT) promoter status (molecular analysis) and BRAF mutation status (immunohistochemical staning) was determined. Outcome data were collected from the patient records.
Results: We included 69 patients; recurrences and/or metastases were seen in 18 and 9 cases respectively. The current data show that tumour thickness >1,5 mm, mitotic figures, ulceration and TERT mutations have an adverse relationship with development of metastasis in the univariate analysis (p-values of 0.002, 0.001,<0.001 and 0.004 respectively). The other histopathologic parameters and the presence of a BRAF mutation showed no relationship with metastasis. None of the parameters were associated with recurrences.
Conclusion: Besides known risk factors including tumour thickness, also ulceration, mitotic figures and TERT mutations showed prognostic value in our cohort.

OFP-15-012
To distinguish IgG4-related disease from granulomatosis with polyangiitis
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Objective: IgG4-related disease (IgG4-RD) is a fibro-inflammatory disease that can affect almost every organ and mimics several immune mediated diseases. Indeed, previous unexplained conditions have now been reclassified as primarily IgG4-RD. Since IgG4-RD localized in the orbital or nasal region remarkably resembles limited granulomatosis with polyangiitis (GPA), IgG4-RD could be an alternative diagnosis in ANCA negative limited GPA.
Method: We present three cases of IgG4-related eosinophilic angiocentric fibrosis of the orbit accompanied with chronic and recurrent nasal symptoms raising the suspicion of limited GPA.
Results: The nasal symptoms varied from recurrent excessive nasal mucus and crusts formation, nasal polyposis, swollen nose to saddle nose. The histology in these cases was inconclusive and

anti-neutrophil cytoplasmic antibodies were negative, however, patients were highly suspect of limited GPA because of clinical presentations and were treated in such a way. Histopathological revision revealed IgG4-related eosinophilic angiocentric fibrosis in all three cases.
Conclusion: These cases confirm eosinophilic angiocentric fibrosis being part of the spectrum of IgG4-RD. Patients suspected of limited GPA should be evaluated for IgG4-RD, especially when diagnosis GPA cannot convincingly be established. The diagnosis is based on clinical presentation, serum IgG4 and histology, the gold standard. Proper diagnosis and treatment is important to prevent manifestation in other organs and to prevent irreversible fibrosis due to the disease.

Wednesday, 6 September 2017, 14:00–16:00, G109
OFP-16 Cytopathology

OFP-16-001
Performance of ProEx C supplemented with HPV genotypic analysis in detecting cervical squamous intraepithelial lesions
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Objective: The clinical usefulness of the ProEx C test (BD) for the detection of cervical intraepithelial neoplasia (CIN) was determined in a multicentre study carried out in Canada, supplemented with HPV genotypic analysis.
Method: The study population comprised of women representing five of the ten Canadian provinces referred to colposcopy for further assessment of cervical cancer risk and follow-up, and those routinely screened. Cervical specimens were collected in PreservCyt and cytology was performed using the ThinPrep method (Hologic), and were processed for HPV genotyping using the Linear Array method (Roche Molecular System). Histology confirmed CIN served as the disease endpoint to assess the test performance.
Results: ProEx C was positive in 39 % (634/1625). ProEx C detecting CIN was best found at CIN2+ with a concordance rate of 73.5 % (95 % CI: 72.4–74.6). The overall positive rate of HR-HPV was 69.8 % (1135/1625), with a concordance of 54.0 % (95 % CI: 52.8–55.3) for detecting CIN2+. The sensitivities of ProEx C and HR-HPV in detecting CIN2+ lesions were 74.2 and 95.3 % while the specificities were 73.3 and 39.3 %, respectively. A significant correlation between ProExC and HR-HPV in terms of detecting CIN2+ lesions was found ($p = 0.044$).
Conclusion: ProEx C was found to be more specific but less sensitive than HR-HPV marker in detecting CIN2+ lesions. ProEx C may have the potential to serve as a useful adjunct test for the detection of CIN2+ lesions in cervical cancer screening.

OFP-16-002
Intra-institutional second opinion diagnosis may reduce unnecessary surgery for indeterminate thyroid fine-needle aspirates
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Objective: Although fine-needle aspiration (FNA) is a highly cost-effective diagnostic procedure, a significant proportion of thyroid nodules are classified as indeterminate. Thus, a second diagnostic opinion given by an outside expert pathologist is a common practice that facilitates more appropriate clinical management. Conversely, little is known about the role of intra-institutional second opinion diagnosis (iSOD) that is usually informally performed in-house and may improve the diagnosis of indeterminate thyroid nodules requiring surgery.
Method: To assess the contribution of iSOD, a retrospective series of 34 thyroid FNAs diagnosed as follicular neoplasm/suspicious for follicular neoplasm (FN/SFN) with matched histological follow-ups and a malignancy rate of 17.6 % was selected and independently reviewed by two cytopathologists (CYT1 and 2). Cases with discrepant diagnoses were referred to a third in-house senior cytopathologist for the iSOD. The malignancy rates obtained after single independent reviews and iSOD were compared.
Results: MR obtained after CYT1 and 2 re-screening was similar (14.28 and 19.04 %, respectively) and did not improve the original MR (17.64 %). Conversely, after the iSOD of discrepant diagnoses, the overall malignancy rate increased up to the 27.27 %.
Conclusion: Intra-institutional second opinion practice potentially avoids unnecessary surgical procedures and maximizes the detection of malignant cases diagnosed as FN/SFN.

OFP-16-003
Risk stratification of salivary gland lesions on cytology based on the proposed Milan System for reporting salivary gland cytopathology: A pilot study
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Objective: Fine-needle aspiration (FNA) is widely used for the initial diagnosis of salivary gland nodules. The recently proposed Milan system aims to standardize the reporting of salivary gland cytopathology. Studies regarding the risk of malignancy (ROM) for the proposed categories are evolving. Our retrospective study aims to re-categorize salivary gland lesions using the proposed Milan system and calculate evidence based ROM.
Method: 186 salivary gland FNAs from 175 patients over 5 years (2011–2016) at Weill Cornell Medicine/New York Presbyterian Hospital were identified. 105 of these FNAs had histologic or flow-cytometry follow up. The mean age was 59 (range 22–99) years, and M:F is 1:1.3. Samples were processed with liquid-based cytology alone, or in combination with air-dried Diff-Quik or Ultra fast stained, or alcohol fixed Papanicolaou-stained smears. Cellblock study was used where available. The final cytology were re-categorized into 6 major categories by two independent cytopathologists, as 1- Non-diagnostic, 2- Non-neoplastic, 3- Atypia of undetermined significance, 4a-Neoplastic, benign and 4b- neoplastic, uncertain malignant potential, 5-suspicious for malignancy, and 6- malignant. The risk of malignancy (ROM) and the overall ROM (OROM) for each diagnostic category were determined.
Results: There was near perfect agreement on category assignments. The results for OROM in the categories 1, 2, and 3, were 5, 9, and 15 %, respectively. The ROM for neoplastic lesions and above, 4a, 4b, 5 and 6 was approximately 9, 26, 100, and 95 %, respectively.
Conclusion: Categorization of salivary gland cytology is feasible and can help standardize reporting and stratifying cases pre-operatively, for effective patient management.

OFP-16-004
Biochip as a new perspective in cytological diagnostics of serous effusions
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Objective: The purpose of this study was to show advantages of application of fluorescent immunocytochemistry (FICC) using biochip in serous effusions.
Method: 86 specimens of serous effusions were investigated. At first all the slides were prepared using Cytospin-3 and evaluated cytologically. Then immunocytochemical assay was performed using biochip and fluorescent microscope. Biochip is a device with 15 equal individual cells.

Each cell has a transparent bottom with adhesive cover containing MA Ber-EP4, conjugated to fluorochrome Cy3. And finally all the material was stained conventionally in azure-eosin for reanalysis.
Results: In 86 cases, 35 effusions were malignant, 19 had only reactive mesothelial cells and 32 were suspicious for malignancy. In 35 cases, 33 were confirmed by biochip-FICC as metastatic effusions and 2 had negative ICC. One of them was subsequently characterized as non-specific effusion, the other one turned out to be a metastasis of high-grade serous ovarian cancer. In 19 (negative for malignancy) cases, 12 had no reactions with Ber-EP4, but 7 were Ber-EP4-positive, that confirmed the presence of tumour. The other 32 specimens (37 % of all cases) required FICC, and tumour cells were identified in 15 of them.
Conclusion: FICC on biochips is a reliable and rapid method for cytological diagnostics of serous effusions. This technique allows to identify few cells and small groups of cells that may be missed in conventional cytology, thereby reducing the frequency of hyper- and hypodiagnosis. Ease of use is also one of the advantages—It doesn't take much time and has no complications in preanalytic phase.

OFP-16-005
Predictive accuracy of thyroseq v2 for malignant thyroid nodules among Bethesda-III cytology subcategories: Atypia of undetermined significance (AUS) and follicular lesion of undetermined significance (FLUS)
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Objective: The objective of this study is to determine the accuracy of ThyroSeq v.2 testing panel in predicting malignancy in Bethesda-III thyroid nodules subcategories AUS and FLUS.
Method: In this prospective cross-sectional study, we compared 258 thyroid nodules with Bethesda-III diagnosis and the corresponding ThyroSeq v.2 testing form January 2015- March 2017. Definitive histopathologic diagnosis was the gold standard for this study.
Results: Of 203 nodules (72 % AUS; 28 % FLUS), 36 % had positive Thyroseq v.2 testing; 40 % in AUS vs. 26 % in FLUS ($p = 0.07$). Of 45 nodules undergoing resection, 94 % of AUS and 75 % of FLUS proved malignant, with odds-ratio of 10.5 ($p = 0.02$) and 1.8 ($p = 0.59$), respectively, In AUS, positive testing identified 15/16 malignant lesions, showing 93.8 % (95%CI,69.8 %–99.8 %) sensitivity, 41.2 % (95%CI,18.4 %–67.1 %) specificity, 60 % (95%CI,38.7 %–78.9 %) positive predictive value, and 87.5 % (95%CI, 47.3 %–99.7 %) negative predictive value. In FLUS, positive testing identified 3/4 malignant lesions, having 75 % (95%CI, 19.4 %–99.4 %) sensitivity, 37.5 % (95%CI, 8.52 %–75.5 %) specificity, 37.5 % (95%CI, 8.52 %–75.5 %) positive predictive value, and 75 % (95%CI, 19.4 %–99.4 %) negative predictive value.
Conclusion: ThyroSeqv.2 test improves accurate classification and malignancy prediction with significantly high sensitivity and negative predictive value in AUS but not FLUS nodules. Bethesda-III sub-categorization may improve the accuracy of diagnosis and management recommendations.

OFP-16-006
Liquid-based Pap test and expression of biomarkers in a residual media in postmenopausal women
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Objective: This study was conducted to compare the correlation between Pap smear and mRNA gene expression analysis by quantitative PCR in postmenopausal women. The aim was to evaluate the possibility of differentiation CIN 2+ from CIN1 or less in postmenopausal women based on the the expression of the 21-gene panel mRNA measurement by quantitative PCR in residual material Pap test CellPrep
Method: 17 postmenopausal women had subsequent biopsies performed within 3 months of obtaining the cytodiagnosis. All cases were tested for the expression of the 21 genes (Ki-67, STK-15, CCNB1, CCND1, MYC, MYBL2, P16INK4A, PTEN, BIRC5, BCL2, BAG1, TERT, NDRG1, ESR1, PGR, HER2, GRB7, MGB1, MMP11, CTSL2, CD68) in a media from the vial after Pap test CellPrep
Results: The histological examination revealed: CIN1-CIN3 (10 patients), endocervical adenocarcinoma (1 patient), normal epithelium/benign tissue changes of the cervix (6 patients). We observed that 2 (11.76 %) cases of LSIL was false positive and the positive predictive value for the CellPrep Pap test was 83.3 %. The discriminant analysis revealed the opportunity for distinguishing of specimens with and without CIN 2+ by mRNA gene expression analysis of 2 genes. The total percentage of the predicted classifications is 100 %
Conclusion: Evaluation of the expression of 21 genes panel, complementary to the cytological preoperative diagnosis of precancerous processes and cervical cancer in postmenopausal women in the media of liquid-based cytology allows a high precision differential diagnosis of 2 clinically important groups: the CIN 2+ and the CIN1 or less

OFP-16-007
Liquid-based cytology of fallopian tube smears in intraepithelial precancerous lesions diagnostics
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Objective: The goal of the study was to evaluate diagnostic value of liquid-based cytology for benign and precancerous lesions of the tubal epithelium
Method: 23 fallopian tubes from 14 patients (mean age 47,3 ± 13,3 years) with ovarian high-grade serous carcinoma (HGSC) ($n = 6$), serous borderline ovarian tumours (SBOT) ($n = 7$), benign ovarian tumours ($n = 10$) were analyzed using liquid-based cytology, histology, immunocytochemistry (ICC) (bcl-2 expression) and immunohistochemistry (IHC) (p16 and Ki-67 expression). A chi-square test for a contingency table was used for statistical analysis.
Results: Results. Hypocellular smears were revealed in 48 % of cases, normocellular in 32 % of cases, and hypercellular - 20 %. Marked anysonucleosis were revealed in 16 % of cases, moderate - in 24 %, and slight - in 40 %. Marked irregularities of the nuclear membrane were found in 8 % of cases, moderate - in 16 %, slight - in 40 %, and were absent in 28 % of cases. Varied nuclear shape was found in all groups, but most often it was detected in patients with HGSC (in 83 % of cases) and less often - in patients with benign tumours (in 30 % of cases). Statistically significant differences were found for two studied parameters only: nuclear polymorphism and irregularities of the nuclear membrane, which significantly more often were found in patients with HGSC ($p < 0.05$). Histologically STIC and more than 10 SCOUTs significantly more often were found in HGSC, whereas papillary tubal hyperplasia—in borderline ovarian tumours ($p < 0.01$).
Conclusion: Our study has demonstrated that liquid-based cytology can be used for the determination of fallopian tube epithelial malignant and benign cells and verification such precancerous intraepithelial lesions such as SCOUT and STIC. Thus, this method can play a leading role in ovarian cancer screening. The study results carried on the funds received from RFBR (16 16-34-00666 / 16).

OFP-16-008
The pathologist in the clinic: Pathologist-performed ultrasound guide thyroid fine needle aspiration cytology (UG-FNAC) improves adequacy and sensitivity
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Objective: To compare thyroid UG-FNAC performed by pathologists and endocrine surgeons at a university hospital clinic.
Method: A 2.5-year retrospective review of thyroid UG-FNAC between October 2014 and February 2017. One hundred and thirty four patients were identified that had both thyroid surgery with histology and preoperative cytology for a total of 163 thyroid nodules. UG-FNAC was performed 184 times by either (i) a surgeon with no rapid on-site evaluation (ROSE) of sample adequacy (79 FNACs), (ii) a surgeon with ROSE by a pathologist (29 FNACs), or (iii) a pathologists alone (76 FNACs). The results were evaluated with respect to the three practice situations.
Results: Inadequacy rates were 19,2 % for surgeons without ROSE, 3,8 % for surgeons with ROSE, and 2,5 % for pathologists. For neoplastic lesions, pathologist UG-FNAC had higher sensitivity (97,8 % vs. 61,2 %), specificity (93,1 % vs. 82,8 %) compared with surgeon UG-FNAC without ROSE. When compared with surgeon UG-FNAC with ROSE, pathologist UG-FNAC had higher specificity (93,1 % vs 53,9 %). For malignant lesions, pathologist UG-FNAC had higher sensitivity (83,3 %), than both surgeon UG-FNAC with (60,0 %) or without ROSE (33,3 %).
Conclusion: Pathologist-performed UG-FNAC of thyroid nodules results in fewer non-diagnostic samples and improves the accuracy of the cytological diagnosis.

OFP-16-009
Comparison of cytological characteristics and nuclear structure analysis of the thyroid's follicular patterned lesions and classical papillary thyroid carcinoma
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Objective: Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is cytologically different from classical papillary thyroid carcinoma (PTC) and follicular neoplasms (FN). We focused on the cytologic features, and morphometric nuclear texture analysis of NIFTP, FN, and and classical PTC.
Method: One hundered thirty two patients' cytologic and histopathologic slides (38 NIFTP, 21 invasive follicular variant papillary thyroid carcinoma (IFVPTC), 24 classical PTC, 19 follicular adenoma (FA), 10 follicular carcinoma (FC) and 20 adenomatous nodule (AN) were included in the study. The cytology slides were evaluated for 28 parameters. Thirty cells selected from ten cases of each group went for nuclear morphometric and texture analysis.
Results: The PTC and IFVPTC group cases were similar in almost all parameters and the IFVPTC cases contain most of the features of the PTC in a slightly lesser amount. FC shows more distinct microfollicular pattern than NIFTP and can be distinguished from NIFTP by significant fibrous tissue, anisonucleosis, and intranuclear cytoplasmic inclusion. Significantly increased granularity was observed cytologically between NIFTP and FA and AN.
Conclusion: NIFTP and FA, can be differentiated cytologically. NIFTP was morphometrically located between the invasive PTC (IFVPTC and PTC) and FN group, with similar features to the FN group.

OFP-16-010
Qualifiers of atypia in the cytologic diagnosis of thyroid nodules are associated with different BRAF, RAS, RET/PTC and PAX8/PPARg alterations
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Objective: In the Bethesda System for Reporting Thyroid Cytopathology, Atypia/Follicular Lesion of Undetermined Significance (AUS/FLUS) category has a low risk of malignancy (MR) that varies due to specific diagnostic "qualifiers". Several studies have analyzed the utility of these qualifiers to further stratify the MR of AUS/FLUS FNA. However, little is known about the prevalence of the alterations in the genes frequently involved during thyroid oncogenesis among the different AUS/FLUS qualifiers.
Method: We have prospectively tested on a series of 162 thyroid FNAs diagnosed as AUS/FLUS the most common BRAF, HRAS, NRAS, KRAS mutations and PAX8/PPAR-γ, RET/PTC1 and 3 rearrangements on a Real-Time based PCR platform. Moreover, we have investigated the association between the different AUS/FLUS qualifiers (namely Architectural, Cytologic and Hurthle cells atypia) and the corresponding mutational status.
Results: A significant difference among the AUS/FLUS qualifiers was observed only for the wild-type (WT) status (p-value <0.0001) and BRAFV600E (p-value < 0.0001) mutations. Particularly, the AUS/FLUS cases featuring Architectural and Hurthle cells atypia were associated with a WT status whereas the BRAFV600E mutation was associate with the Cytologic Atypia.
Conclusion: The association between BRAFV600E mutation, a specific marker for papillary thyroid cancer, and Cytologic Atypia confirmed that this latter AUS/FLUS qualifier is more predictive of a malignant outcome.

OFP-16-011
Endoscopic ultrasound- guided fine needle aspiration cytology (EUS-FNAC) of pancreatic lesions in the Indian Subcontinent
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Objective: To reclassify pancreatic lesions based on proposed classification of Papanicolaou Society of Cytopathology and their histopathological correlation wherever available.
Method: A total of 549 cases were included during June 2010 to March 2017.
Results: We classified Pancreatic lesions on the basis of recent guidelines given by the Papinacolaou society of Cytopathology . The categories of Pancreatic lesions were, category I (Inadequate) (n = 43), category II (Negative for malignancy) (n = 105), category III (atypical) (n = 16), category IVA/IVB (Neoplastic: Benign/Others) (n = 73), category V (Suspicious for malignancy) (n = 48) and category VI (Positive for Malignancy) (n = 264).Out of 549 samples, 506(92 %) were adequate for reporting and 43(8 %) were inadequate. In 52 cases surgical specimen correlation was available, based on which the. sensitivity of EUS FNA cytology was 82 % and specificity was 100.00 % . The cell block with immunocytochemistry was done in 28 cases with most of the cases being neuroendocrine tumour (NET) (n = 09) and solid pseudopapillary neoplasm (SPN) (n = 07) with specificity and sensitivity reaching upto 100 %.
Conclusion: Cell block preparation is recommended in pancreatic lesions specially for subtyping of NET and SPN. EUS-FNAC is highly accurate technique and its use, allied with standard Papanicolaou classification system may contribute to an early diagnosis and tailored patient management.

OFP-16-012
Risk of preneoplastic and neoplastic cervical lesions in HPV-positive/cytology negative women from a cotest cervical screening study of 5.053 women in Madrid. Results from a 12 to a 30-month follow-up
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Objective: To determine the risk of developing a preneoplastic cervical disease in the 5,9 % (n = 299) of women attending a cotest study with positive high-risk HPV (hrHPV) tests and negative cytology

Method: Women were advised to have a colposcopy after the baseline results and to undergo a 12-month follow-up according to EU guidelines. Cytology was performed with ThinPrep® and mRNA of hrHPV was detected by APTIMA® (AHPV).
Results: There were 195 (65,2 %) AHPV-positive/cytology-negative women with initial colposcopy and biopsy. From those, 189 had adequate biopsies, yielding cervical disease in 48,7 % (92) of cases, including 30 cases (15,9 %) of CIN2+ lesions. Follow-up at 12–24 months revealed 4 additional cases of high-grade preneoplastic lesions in cases with a previous negative biopsy and 2 CIN2+ biopsies in women with a previous CIN1 biopsy, including one adenocarcinoma in situ (AIS). Only 3 of these women had cytological abnormalities in the follow-up and 44,4 % were younger than 35 years
Conclusion: The risk of harbouring a CIN2+ cervical lesión in AHPV-positive women without cytological abnormalities raises to 15,9 % at baseline colposcopy and increases up to 19 % with adequate follow-up. Due to the elevated risk of high-grade lesions in young women, HPV testing seems advisable before the age of 35

Poster Sessions

Sunday, 3 September 2017, 09:30–10:30, Hall 3
PS-01 Breast Pathology

PS-01-001
HER2, chromosome 17 polysomy and DNA ploidy status in breast cancer; a preclinical and clinical study
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Objective: Human epidermal growth factor receptor-2 (HER2, located on chromosome 17) amplification assessment is widely used for guiding systemic treatment approaches in both primary and metastatic breast cancer. In general, a double probe fluorescence in situ hybridisation (FISH) test is used, whereby also loss and gain of the centromere of chromosome 17 can be observed. This can be interpreted as monosomy or polysomy of chromosome 17, respectively. With this present study we wanted to explore the presence of polysomy of chromosome 17 and its impact on HER2 testing.
Method: A double probe HER2 FISH test was performed on metaphase spreads and agarcyto blocks of ten human cancer cell lines. In addition, HER2 immunohistochemistry, DNA ploidy status assessment and a multiplex ligation-dependent probe amplification (MLPA) test was performed on all 10 cell lines. Furthermore, dual probe HER2 FISH and DNA ploidy status assessment was performed on a selection of 97 breast cancer cases.
Results: Copy number gain of chromosome 17 was observed in metaphase spreads in eight of ten cancer cell lines, accompanied by DNA aneuploid gains in seven. There was no polysomy of chromosome 17 in any of the cancer cell lines. Patients' breast cancer samples showing ≥3 CEP17 signals using dual probe FISH, strongly correlated with aneuploid gains of the tumour (91.1 %; $p < 0.001$).
Conclusion: This study has shown that copy number gain of CEP17, which is encountered regularly in HER2 testing of breast cancer, is not due to gain of only chromosome 17, but is a result of DNA aneuploidy of the tumour with gain of several chromosomes. As aneuploidy is associated with poor clinical outcome, also within grade 1 and grade 2 tumours, this might be used for therapeutic decision-making in the future.

PS-01-002
Role of core needle biopsy in diagnosis and management of papillary lesions of breast
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Objective: The present study was aimed to compare the diagnosis of papillary lesions of the breast on core needle biopsy (CNB), with their subsequent excision biopsies. These findings were used to identify a subset of patients with papillary lesions in which surveillance rather than excision could be considered.
Method: Retrospective analytical–descriptive study done from June 2011 to February 2017.
Results: : During this period we received 1329 breast CNBs of which 131 were diagnosed as papillary lesions. In 81 of these cases excision was performed. On CNB, the papillary lesions were categorized as intraductal papilloma (n = 47, 58 %), atypical papillary lesions (APL) based on atypical morphology and ambiguous immunohistochemistry (IHC) (n = 5, 06 %) and papillary carcinoma based on atypical morphology and confirmatory IHC (n = 29, 36 %) . On follow up excision biopsy, the positive predictive value (PPV) was 13 % for intraductal papilloma, 80 and 100 % respectively for APL and papillary carcinoma.
Conclusion: APL or papillary carcinoma on CNB mandates excision while the benign papillomas can be managed conservatively based on multidisciplinary review and individual institution's upgrade rate. It is one of the largest study on papillary lesions done in Indian population as per our knowledge.

PS-01-003
The role of core needle biopsy in diagnosis of metaplastic carcinoma of breast in the developing countries
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Objective: To emphasie the importance of core needle biopsy (CNB) in diagnosis of metaplastic carcinoma of breast.
Method: Retrospective descriptive study done from January 2013–March 2017.
Results: During this period we received 2309 cases of breast carcinoma, of which 09 were metaplastic carcinoma (0.4 %) with a median age of 53 years. These cases were 07 cases of spindle cell carcinoma and 02 cases of squamous cell carcinoma. All these cases were diagnosed on core biopsy using immunohistochemical markers; CK (AE1 + AE3), HMWCK, CK5/6, p63, ER, PR and Hercept. 02 of such spindle cell carcinoma were associated with DCIS. In 07 out of 09 cases, radiology was suggestive of phyllodes tumour with multiple lobulated masses.
Conclusion: Core needle biopsy is an important technique which can be used to start early patient therapy in metaplastic breast carcinoma. CNB with immunohistochemistry differentiates spindle cell tumours from metaplastic carcinomas whch differs in treatment and prognosis of the patients.

PS-01-004
Clinicopathological features of microinvasive breast cancer
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Objective: Microinvasive breast cancer (MIBC) is defined as invasive carcinoma ≤1 mm. It is usually diagnosed in association with ductal carcinoma in situ (DCIS). We aim to evaluate the clinicopathologic features of MIBC and the incidence of sentinel lymph node (SLN) metastasis.
Method: All cases of MIBC diagnosed between 2008 and 2015 were retrieved. Clinicopathological data was analyzed. Descriptive statistics, Chi-square, Fisher and Mann-Whitney tests, Kaplan-Meier curves and log-rank test were performed.

Results: 128 patients were identified; the majority of cases presented with microcalcifications. 126 cases were associated with DCIS with a median size of 3.7 cm (0.6–11.5 cm); 58.6 % were high grade. The average number of foci was 2 (1–19) and 55.5 % had a single focus. Median size of DCIS was significantly superior in the multiple foci group ($p = 0.014$). Lymphovascular invasion (LVI) was associated with SLN positivity ($p = 0.001$). During follow-up, one distant relapse was found (SLN+). Five-year survival rate was 98.5 %, disease-free survival was 98.8 % and they were not associated with the number of invasive foci.
Conclusion: MIBC is usually associated with extensive, high grade DCIS. Multifocal invasion was not associated with worse prognosis. Incidence of SLN positivity is low (1.6 %) and was significantly associated with LVI. SLN assessment may not always be necessary and should be individualized.

PS-01-005
Breast cancer in women aged 25 years and younger: Pathological characteristics and molecular subtypes in a series of 11 cases
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Objective: Breast cancer is the most frequent cancer in women worldwide. It has different clinical and pathological features and a more aggressive behavior in young women. The purpose of this study was to analyze the pathological characteristics of breast cancer in women who were ≤25 years old at the time of diagnosis.
Method: Between 1995 and 2017, 11 tumours samples from patients aged ≤25 years with the diagnosis of breast cancer were retrieved from the archives of Hospital Universitario La Paz, Madrid, Spain.
Results: In our series, ten cases (90.9 %) were diagnosed as invasive ductal carcinoma, and 90 % of them were of histological grade 3. Mean age was 22.7 years (range 17–25). Mean tumour size was 3.04 cm (range 1.2–8). Lymph node metastases were present in 27.2 % of cases. Estrogen receptor (ER) and progesterone receptor (PgR) were positive in 54.5 and 40 % of cases, respectively. Overexpression of HER2 was observed in 30 % of cases. Mean Ki67 index was 42.75 % (range 10–70). Molecular classification showed following phenotypes: Luminal A, 10 %; Luminal B/Her2-, 20 %; Luminal B/Her2+, 30 %; and basal-like, 40 %.
Conclusion: Breast cancer in very young women shows larger size, high histological grade, and ductal histology. Molecular classification reveals a high frequency of basal-like subtype.

PS-01-006
Methylation pattern of long interspersed nuclear element-1 (LINE-1) in different tissues of patients with breast cancer
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Objective: Long interspersed nuclear element 1 (LINE-1) retrotransposons have fluctuating activity during cancer development and progression. Their activity is associated with genomic instability and largely dependent on methylation status. In this study we examined the patterns of LINE-1 methylation in different tissues of patients with breast carcinoma.
Method: Patients with biopsy-proved ductal invasive carcinoma of breast and no neuadjuvant therapy were selected for the study. Peripheral blood was obtained before surgical intervention. Tumour cells and normal breast tissue were collected by microdissection from sections of the post-operative breast specimen. Genomic DNA was extracted and methylation levels of LINE-1 were investigated by the combined bisulfite restriction analysis (COBRA-LINE1).
Results: LINE-1 methylation status was not uniform in different tissues of the same patient. In most tumours unmethylated sequences predominated. While some blood DNA samples contained exclusively methylated elements. Samples of normal breast tissue showed lower LINE-1 methylation levels comparing to blood samples and in some cases had LINE-1 methylation pattern similar to that of tumour cell DNA.
Conclusion: LINE-1 hypomethylation is associated with cancerous properties of the cells. Most likely there are some locally-acting factors altering LINE-1 methylation levels implicated in development and progression of tumours or LINE-1 hypomethylation is a secondary event following malignant transformation.

PS-01-007
Meningeal carcinomatosis in breast cancer patients: Clinicopathological aspects and survival
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Objective: We analyzed clinicopathological aspects and survival of 56 patients with(w/) meningeal carcinomatosis(MC), a rare complication in breast cancer(BC), diagnosed in the cerebrospinal fluid.
Method: We evaluated age, histologic subtypes, molecular markers and clinical outcome of women w/MC diagnosed between 1990 and 2016.
Results: Mean age: 50 years-old; thirty-two ≤50 (57 %). Forty-two carcinomas (75 %) were invasive not otherwise specified(NOS), 6 cases lobular (11 %). Twenty-seven (54 %) were grade 2 and twenty-one (42 %) grade 3. Forty tumours (71 %) were estrogen receptors positive(+). Eight (19 %) of 42 ERBB2 evaluated tumours were + and 7 were triple negative(TN). Fifty-five patients (98 %) died; follow-up = 61 months. The mean time between BC and MC diagnosis was 58 months. Mean survival since MC diagnosis was 3.5 months. Women >50 years-old had a mean survival of 2.1 months and ≤50 of 4.1 months. The mean survival of lobular carcinomas was 15 months (NOS 2.2 months). Grade 3 carcinomas and ERBB2+ tumours had 1.4 months of mean survival. TN tumours survived <1 month.
Conclusion: The outcome of BC patients w/MC is poor. Women ≥50 years-old lived less than younger patients. After MC diagnosis: lobular carcinomas had longer survival; grade 3 carcinomas and ERBB2+ had the same low survival; TN had the lowest survival.

PS-01-009
Challenges and pitfalls in immunohistochemical evaluation of c-erbB-2 in breast cancer
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Objective: Breast cancer is the most common and, if remain untreated, a lethal cancer among women. Improvements concerning the individual treatment modalities play a great role in prognosis and disease free survival. As c-erbB-2 expression directly affects the treatment of breast cancer, this feature is routinely evaluated by immunohistochemistry in many laboratories. However, the immunohistochemical evaluation of c-erbB-2 possesses several challenges and pitfalls mainly related to the c-erbB-2 clones used, variabilities among the observers, and some morphological characteristics of tumour. This study is designated to investigate the differences between the two frequently used c-erbB-2 clones, CB11 and 4B5.
Method: C-erbB-2 scores of 218 breast cancer cases were overviewed retrospectively for 18 months' period of time.
Results: Consequently, there were much more 2+ scores with clone-CB11 compared to that of 4B5. Afterwards, by using silver-based in-situ hibridization technic, HER2 gene amplification was detected in 30 % of cases with score 2+ with clone-CB11, while it was 48 % of cases with score 2+ with clone-4B5.

Conclusion: In terms of c-erbB-2 evaluation in breast cancer, clone-4B5 is not only a more reliable marker than clone-CB11, but it also reduces the number of in-situ hibridization tests which are time consuming and have higher costs, as well.

PS-01-010

Interleukin 8 in triple-negative breast cancer

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Objective: Triple-negative breast cancers (TNBC) are known difficult to treat due to the lack of obvious therapeutic targets. A possible mechanism explaining the TNBC resistance to all types of therapy could be the activation of cancer stem-like cells (CSCs). In turn, interleukin-8 (IL-8) is considered as the main promoter of CSCs activity. The aim of the study is to evaluate the real synthesis of IL-8 in tissues of patients with TNBC.
Method: The primary cultures of TNBC were obtained from tumour specimens of 18 patients. The IL-8 level in the culture supernatants was determined by ELISA. The presence of IL-8 cognate receptor, CXCR1, was detected by immunohistochemistry both in primary cultures and tumour tissues.
Results: High IL-8 concentrations (700–7000 pg/ml) were found in 6 of 18 TNBC culture supernatants (33 %). Four cases showed relatively low IL-8 levels (50–250 pg/ml) and IL-8 was undetectable in 8 tumour supernatants (44 %). All tumours exhibited high levels of IL-8 had a prominent immunohistochemical reaction for CXCR1. Moreover, all these cases were strongly associated with multiple metastases. The tumours displayed low or undetectable IL-8 level had variable reactiveness for CXCR1 and single or no metastases.
Conclusion: The obtained difference in the IL-8 synthesis suggests the heterogeneity of triple-negative subtype and could contribute to the search of therapeutic targets for TNBC.

PS-01-011

Evaluation of tumour-infiltrating lymphocytes (TILS) and PD-L1 expression in breast cancer of young women

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Objective: To evaluate TILs and PD-L1 in invasive breast carcinomas of young women.
Method: All cases of invasive breast carcinoma of women younger than 40-years-old, diagnosed between 2011 and 2016 in our Pathology laboratory (UOI) were included in this study. A representative haematoxylin-eosin slide was evaluated for TILs. Four-μm thick sections were processed for immunohistochemistry, using the following antibodies: CD3, CD8, PD-L1. Evaluation was based on published protocols [high TILS >50 %, Allred score for PD-L1 in tumour cells (TCs) and immune cells (ICs)].
Results: Forty-five invasive carcinomas (NST) were included in the study. Grade, ER/PR and HER2 status were recorded. There was no statistically significant correlation between TILs and grade or HER2 status ($p = 0.076$, $p = 0.124$ respectively, Gamma statistics). All triple negative (TN) tumours (4/45) and 50 % (6/12) of HER2+ tumours had high stromal TILs. There was agreement between CD3 and CD8 density (weighted kappa coefficient = 0.951, $p < 0.001$). Regarding PD-L1, 10/45 tumours (22 %) were positive in TCs, while 47 %(21/45) were positive in ICs. Ninety percent of TC-PD-L1 + tumours were also IC-PD-L1+. Of TC-PD-L1+, 90 % had high TILs, including all 4 TN tumours. There was no statistical correlation between PD-L1 and HER2 status.
Conclusion: Breast cancer in young women has a distinct immune cell profile.

PS-01-012

The metastatic potential of grade 1 breast carcinoma of no special type: A deep insight into putative molecular mechanisms

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Objective: Among breast carcinoma of no special type (BC-NST), grade 1 tumours have the best prognosis. However, rarely they metastasize to the axilla, suggesting a more aggressive behaviour. Our study aimed to uncover the mechanism responsible for the dissemination of tumour cells of grade 1 BC-NST into axillary lymph nodes to better understand lymph node metastasis phenomenon in breast cancer and stratify the patients.
Method: Whole-exome sequencing technique was used to analyze 10 formalin fixed, paraffin embedded grade 1 BC-NST, 5 with lymph node metastasis and 5 without, matched for size. Biostatistical analysis compared the molecular profiles of the selected cases by Enlis Genome Research software and Cravat application.
Results: Mutational profile analysis showed an increased mutational rate in metastatic tumours compared to non-metastatic ones. In particular, we identified a higher number of molecular alterations in tumour suppressors and oncogenes shared by all tumours in the metastatic group compared to the non-metastatic one.
Conclusion: These results suggest that metastatic grade 1 BC-NST have a higher genomic instability with most of the molecular alterations present in genes implicated in cancer. Further analysis will be performed to confirm the data obtained and to construct a genomic profile associated to the metastatic phenotype.

PS-01-013

Prognostic value of CD8+ tumour infiltrating lymphocytes (TILs) in male breast cancer

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Objective: To date, the prognostic value of CD8+ CTLs in male breast cancer have not been evaluated. The objective of the current study was to examine the prognostic value of CD8+ T-cell infiltration in male breast cancer (MBC).
Method: Tumour-infiltrating CD8+ lymphocytes were assessed by immunohistochemistry on 80 male breast tumours. Absolute numbers of CD8+TILs were counted and classified as 'intratumoural' if seen in direct contact with tumour cells, 'stromal' if they were not in direct contact with tumour cells and 'peritumoural' if seen at the invasive margins.
Results: Immunostainings showed higher numbers of CD8+CTLs in the stroma and tumour edge than in the tumour nests. There was significantly different disease free survival (DFS) for patients with stromal CD8 + CTLs positive infiltrate score. Both Intratumoural and Peritumoural CD8+ T cell percentage was positively correlated with large tumour size ($p = 0.05$ and $p = 0.002$ respectively).The total number of CD8+ cells was positively correlated with molecular subtypes ($p = 0.005$).We also performed multivariate analyses and confirmed that stromal tumour-infiltrating CD8+ T cell levels had independent effects on DFS.
Conclusion: These results suggest that tumour-infiltrating CD8+ T lymphocytes have antitumour activity as judged by their favorable effect on MBC patients and could potentially be exploited in the treatment of MBC.

PS-01-014

External quality assurance of HER2 in situ hybridisation (ISH) testing - evaluation of the changes in the UK National External Quality Assessment Scheme (NEQAS) over 8 years and the reflection on participant performance

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Objective: UK NEQAS operates a scheme for assessing laboratories performing HER2 ISH testing. Since its introduction further improvements have been made to the ISH module including the introduction of a more statistically robust scoring method. The objectives of this study were to assess participant's performance over time and evaluate change in testing methods.
Method: Data from NEQAS reports were analysed for performance - (1) across time; (2) in relation to changes in the scheme; and (3) across the assay systems.
Results: Over the most recent 2.5 years, an average of 6.7 % of participant results were classified as 'excellent', 60.1 % as 'acceptable', 24.4 % as 'borderline' and 8.7 % as 'unacceptable'. The preceding 2 years where a different scoring system was used demonstrated a higher unacceptable rate of 15.3 %. In the years prior to this where cell lines were used instead of human tissue, the mean unacceptable rate of participants was 15 %. The impact of the assay method used on laboratory performance showed that Fluorescence ISH based methods outperformed colorimetric ISH methods (mean pass rate 81 % vs 61 %).
Conclusion: Participation in an EQA scheme is essential for demonstrating competency in HER2 ISH testing. However, the performance of laboratories must be considered in the context of module changes over time.

PS-01-015
FGD5 amplification in breast cancer patients is associated with tumour proliferation and a poorer prognosis
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Objective: By means of a combined genomic approach, FGD5 amplification is identified as a driver of proliferation in Luminal breast cancer. We studied FGD5 copy number change in breast cancer tumours, and assessed a possible association with tumour proliferation and prognosis.
Method: We used fluorescence in situ hybridization probes targeting FGD5 and chromosome 3 centromere (CEP3) on formalin-fixed, paraffin-embedded tissue from 430 primary breast cancers and 108 lymph node metastases. All cases were from a cohort of Norwegian breast cancer patients. Using Pearson's Chi-square test, we tested the association between FGD5 copy number status and proliferation (assessed by Ki67 levels and mitotic count). Estimating cumulative risks of death and hazard ratios, we assessed the prognostic impact of FGD5 copy number change.
Results: FGD5 amplification (FGD5/CEP3 ratio ≥2 or mean FGD5/tumour cell ≥4) was identified in 9.5 % of tumours. Amplified tumours had higher mitotic counts and Ki67 levels than non-amplified tumours. After 10 years of follow-up, cases with FGD5 amplification had higher cumulative risk of death from breast cancer than non-amplified cases (48.1 % (95 % CI 33.8–64.7) vs. 27.7 % (95 % CI 23.4–32.6)).
Conclusion: FGD5 is a new prognostic marker in breast cancer, and amplifications are associated with higher tumour proliferation and poorer long-term prognosis.

PS-01-016
Quality of up to 35 years old archival breast cancer tissue in paraffin-blocks for estrogen receptor evaluation
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Objective: Estrogen receptor (ER) positive breast cancer (BC) can have an insidious course with disease-relapse decades after primary surgery. New analysis performed on archived formalin-fixed paraffin-embedded (FFPE) tissue are important for disease-management in late BC-relapse and an important tool in BC-research. However, although loss of immunoreactivity in tissue slides after sectioning has been shown, little is known of the preservation of biomarker-expression in FFPE tumour-blocks. We aim to investigate the quality of immunohistochemical (IHC) ER-evaluation in FFPE-tissue over time (1978–2000).
Method: Tissue-microarrays from a Swedish multicenter cohort of 728 patients with contralateral BC was used for ER IHC-evaluation. BC was studied in three periods (1958–1985, 1986–1993, 1994–2000), and retrospective ER IHC-data was correlated to corresponding prospective ER cytosol-analysis performed on fresh BC-tissue.
Results: The concordance between the original ER cytosol-analysis and the new IHC was substantial (1978–1985: 82 %, (117/142), Kappa 0.63. 1986–1993: 91 %, (194/213), Kappa 0.72. 1994–2000: 86 %, (187/218), Kappa 0.61). Discrepancies were mostly found for tumours with ER-values close to cutoff for one or both of the methods.
Conclusion: FFPE BC-tissue from the late 70s to millennium shows preserved ER-antigenicity up to 35 years later.

PS-01-017
Bcl-2 and Ki67 as specific prognostic markers in estrogen receptor positive breast cancers
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Objective: Breast cancer is a heterogeneous disease, so many biomarkers can be potential predictors in its outcome. The aim of this study is to test the hypothesis that combinatorial assessment of both Ki-67 proliferation index and B-cell Lymphoma 2 (Bcl-2) protein, would provide prognostic information on occurrence of relapses in breast cancer patients.
Method: Immunohistochemical expression of Ki67 and Bcl-2, represented as Ki67/Bcl-2 index, were evaluated in 183 Estrogen Receptor positive breast cancer patients from 2007 to 2012, compared with other clinical-pathologic findings. During the follow up period (45–114 months) recurrences were observed in 36 patients (19.7 %).
Results: A significant correlations were notified between Ki67/Bcl-2 index with age, tumour size, nuclear grade, histologic grade, lymphovascular invasion, progesterone receptor status and expression of p53 protein product ($p < 0,05$). The occurrence of relapses in the group of low Ki67/high Bcl-2 index was lower, compared with the group of high Ki67/low Bcl-2 index breast cancer patients ($p < 0.01$).
Conclusion: The combination of Ki67 and Bcl-2 biomarkers is useful tool in prediction of relapses in Estrogen positive breast cancer patients.

PS-01-018
The scale of androgen expression in triple negative breast cancer
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Objective: The predictive and prognostic role of androgen receptors (AR) expression in patients with breast cancer still remains controversial. Moreover immunohistochemical scale for AR evaluation, as that for ER and PR expression, has not been developed yet. The aim of this study was to determine the intensity of AR expression in the group of triple negative breast cancer, as well as to create AR evaluation scale, similarly to the existing Allred system.
Method: We determined the intensity of expression of AR of 71 FFPE tumour tissue in triple negative breast cancer cases by immunohistochemical method (clone AR441, DAKO).
Results: AR were expressed in 47 cases (66 %). In these cases the staining intensity was homogenous and ranged from weak to strong. In 17

cases (36 %) staining intensity was strong, in 11 (23 %)—weak, and in 40 % - intermediate.
Conclusion: We assessed the expression levels using 4 grades: 0 – no expressive cells; 1- weak expression; 2 – intermediate; 3 - strong expression, similarly to her2/neu expression scale. As a consequence, it is possible to suspect the effectiveness of antiandrogen therapy in patients with triple-negative breast cancer subtype with strong AR expression.

PS-01-019
The EndoPredict gene-expression assay in clinical practice in ER-positive/HER2-negative primary invasive breast cancer: Comparison with standard clinicopathological parameters
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Objective: The aim of this study was to investigate the performance of the EndoPredict assay in clinical practice.
Method: EndoPredict assays from 105 patients were performed at the Molecular Pathology Laboratory of the Hospital Universitario La Paz, Madrid, Spain, between September 2015 and March 2017.
Results: Mean age was 56.5 years (range 33–79). Mean tumour size was 1.7 cm (range 0.4–4). Most tumours were either invasive ductal (80.9 %) or lobular (10.5 %) carcinomas. Twenty cases (19 %) were of histological grade 3. Lymph node metastases were present in 31 patients. The EP molecular score classified 37 patients (35.2 %) as low-risk and 68 (64.8 %) as high-risk. EPclin score (clinicopathological variables combined with EP score) reclassified 55 patients (52.5 %) as low-risk and 50 patients (47.5 %) as high-risk. The high-risk EPclin group was significantly associated with high tumour grade ($p < 0.02$) and high Ki67 ($p < 0.05$). No other associations with clinicopathological parameters were observed. The average turn-around time of test results was 5 days (range 1–17) with 68.7 % of results available in ≤5 working days. Retrospective evaluation of treatment decisions is currently under analysis.
Conclusion: EndoPredict is a useful tool to predict the risk of metastasis in patients with breast carcinoma that can be routinely performed in decentral molecular pathology laboratories.

PS-01-020
The immune microenvironment of ductal carcinoma in situ—a biomarker study
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Objective: The incidence of ductal carcinoma in situ (DCIS) has risen many-fold since the introduction of population-based mammographic screening. A minority of DCIS patients later develop invasive breast cancer. Despite aggressive treatment with surgery and radiotherapy of DCIS, the incidence of higher stage breast cancer has not decreased, suggesting overtreatment of DCIS exists. Therefore it is important to distinguish aggressive from indolent DCIS. As the immune microenvironment plays an important role in cancer progression, we aim to assess the composition of an immune cell marker panel for DCIS lesions in a pilot study.
Method: A representative series of 34 paraffin-embedded DCIS lesions was studied with multispectral immunohistochemical analysis, providing simultaneous detection and quantitation of CD20 + B-cells, CD8 + T-cells, CD4 + T-cells, FoxP3 + regulatory T-cells, CD68 + macrophages and pankeratin.
Results: Multispectral immunohistochemical quantification showed a range of 50 to 600 stromal lymphocytes/mm2 in DCIS cases. CD20 + B-cells, CD8 + T-cells, CD4 + T-cells, FoxP3 + CD4+ regulatory T-cells and CD68 + macrophages were successfully and simultaneously detected in stromal and in situ compartments.
Conclusion: Multispectral immunohistochemical analysis by simultaneous detection of CD20, CD8, CD4, FoxP3, CD68 and pankeratin is feasible in DCIS lesions. This panel will later be analysed in our nationwide DCIS cohort (1989-2004, median follow-up 12,9 years) for correlation with outcome.

PS-01-021
Idiopathic lobular granulomatous mastitis: Retrospective study of 33 cases
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Objective: Our objective is to determine the epidemiological, etiopathogenesis, clinicopathological characteristics and outcome of Idiopathic lobular granulomatous mastitis (ILGM)
Method: It is a retrospective study of 33 cases of ILGM collected from the department of pathology over a 15-year-period
Results: The mean age was 42 years (20 to 65 years).The most common symptom was a breast lump measuring 4 cm in mean size. Both breasts were affected equally. Diagnosis was established after breast biopsy , on tumourectomie or abscess excision specimens. Histological findings revealed granulomatous inflammation centred on mammary lobules with epithelioid and giant cells and without caseous necrosis in the granuloma. After molecular analysis, bacterial DNA was found in 6 cases without being corresponding to the DNA of Corynebactérium. The treatment was based on a surgical excision associated to antibio and corticotherapy .Recurrence was noted in 4 cases with an average follow-up of 25 months.
Conclusion: Idiopathic lobular granulomatous mastitis is a rare chronic inflammatory disease of the breast of unknown etiology. Various factors have been suggested . Recently Infection with Corynebacteria ,a Gram-positive bacteria is incriminated .It has clinical and radiological features, which can mimic breast cancer and lead to delay in definitive diagnosis of IGM,which is pathological and essentially one of exclusion

PS-01-022
Prognostic significance of Forkhead box M1 expression in male breast cancer
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Objective: Elevated expression of FOXM1 in female breast cancer correlates with undifferentiated tumour phenotype and negative clinical outcome. However, to date, whether FOXM1 has any indication for prognosis in male breast cancer (MBC) patients remains unknown. The aim of this study was to investigate the potency of this transcription factor as a prognostic marker in male breast cancer.
Method: Immunohistochemical analysis for FOXM1 was performed in a total of 100 male breast cancer specimens, all with linked clinical outcome data. Kaplan Meier method and Cox proportional hazards analysis were used to relate FOXM1 expression to clinicopathological variables and overall survival (OS).
Results: We observed high expression of the FOXM1 protein in 40 % of MBC samples. FOXM1 overexpression was significantly associated with higher histological grade ($p = 0.05$), lymph node

metastasis ($p = 0.04$), tumour size ($p = 0.05$), and estrogen receptor expression ($p = 0.04$). Patients with FOXM1 expression had a significantly poorer overall survival than those without FOXM1 expression ($p = 0.02$). Multivariate analyses indicated that FOXM1 positivity was an independent prognostic factor for OS ($p = 0.03$).
Conclusion: We have shown the prognostic impact of Forkhead box M1 on male breast cancer patients. Forkhead box M1 inhibition may be a potential therapeutic option for male breast cancer.

PS-01-023
Tumour infiltrating lymphocytes and response to neoadjuvant chemotherapy in invasive breast carcinoma
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Objective: Neoadjuvant chemotherapy(NAC) is used to treat patients with locally advanced invasive breast carcinoma(IBC). A pathologic complete response (pCr)(RCB-0) or minimal residual disease (RCB-1) are strongly associated with improved patient outcome. Tumour infiltrating lymphocytes(TILs) in prechemotherapy breast core biopsies(cbxs) are related to better response rate. The aim of this study was to correlate TILs with response to NAC in our series.
Method: 97 cases of IBC treated with NAC and mastectomy or lumpectomy at Hospital Universitari Son Espases were included. Cases were grouped by molecular type (HR+/HER2-($n = 55$), HR+/HER2 + ($n = 18$), HR-/HER2 + ($n = 5$), and HR-/HER2-($n = 19$)) and by histological grade (G1($n = 13$), G2($n = 50$) and G3($n = 34$)). Prechemotherapy cbxs were available for all cases. TILs in cbxs were calculated by two pathologists following current recommendations. Residual Cancer Burden(RCB) was evaluated in all surgical specimens. RCB-0 and RCB-1 were considered excellent NAC response. Spearman correlation between TIL and RCB was estudied.
Results: Significant overall correlation was found between TILs (range:2 –85 %, median = 11 %) and RCB ($r = -0.262$; $p = 0.010$). By molecular subtypes, there was significant correlation in RH-/HER2- subtype ($r = -0.570$, $p = 0.011$) but correlation was not significant in the other subtypes. By histological grade, there was no significant correlation between TILs and RCB. Higher TILs(>11 %) were correlated with excellent NAC response (OR = 3.317, 95%CI; 1.327–8.294).
Conclusion: Quantification of TILs in cbxs may be useful in predicting response rate to NAC in IBC. TILs could be routinely reported in IBC cbxs to help in the appropriate management and prognostication of patients.

PS-01-025
Value of FOXP3 expression in prediction of neoadjuvant chemotherapy effect in triple negative breast cancer
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Objective: Aim was to examine the value of FOXP3 expression in triple negative breast cancer tumoural cells & tumour infiltrating lymphocytes (TILs) and to elucidate its relation to the extent of neoadjuvant chemotherapy (NAC) response.
Method: 45 of triple negative breast cancer cases were evaluated for NAC response in both tumour and lymph nodes. FOXP3 expression in tumour and TILs was evaluated in the pretherapy biopsies and was correlated with NAC response in breast tumour, lymph nodes as well as other clinicopathological factors.
Results: Breast tumour cells showed FOXP3 positive cytoplasmic expression in (42 %) of cases. High FOXP3 expression percentage was detected in (47 %) of cases. High infiltration by FOXP3 + TILs was detected in (49 %) of cases. High FOXP3 expression percentage was associated with negative lymph node metastasis. High FOXP3 expression percentage and high infiltration by FOXP3 + TILs were significantly associated with complete therapy response in lymph nodes. High FOXP3 expression in tumour cells was associated with high infiltration by FOXP3 + TILs.
Conclusion: FOXP3 may be a good prognostic and predictive marker for TNBC indicated for NAC and can be used for stratifications of TNBC cases indicated for NAC. This study confirmed that tumour cells and the surrounding microenvironment interact with each other. As well, tumour microenvironment can influence the treatment outcomes of TNBC.

PS-01-026
Genomic imbalances and MYB fusion in synchronous bilateral adenoid cystic carcinoma and invasive ductal carcinoma of the breast
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Objective: Case report of a patient having synchronous bilateral breast cancer (BBC) with histologically different tumours: an invasiv ductal carcinoma-NST in the right breast and an adenoid cystic carcinoma in the left breast.
Method: A genome-wide genomic profiling of the tumours was performed.
Results: Our findings indicate that the ACC and IDC-NST had originated independently of each other and that the MYB-NFIB fusion is a specific biomarker for breast ACC.
Conclusion: The incidence of synchronous BBCs has increased with the increased use of magnetic resonance imaging screening of the contralateral breast in women with newly diagnosed breast cancer. Despite the fact that synchronous BBCs are often of the same histological type, they are commonly considered as two separate primary tumours evolving in a similar microenvironment and with the same genetic background.

PS-01-027
Patient-derived xenograft and organoids research models for breast cancer in young women
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Objective: Breast cancer in young women (BCYW,<40 years) is uncommon, yet accompanied by unique challenges, at clinical, personal and social level. Compared to older patients, YW with BC display worse response to standard therapies, higher risk of relapse and lower survival, even in the less aggressive Luminal-histotype. Some key gene-alterations in BCYW may be associated with different rates of proliferation, invasion and metastasis, contributing to the worse outcome in these Luminal subtype (Lum-BCYW) patients.
Method: We have collected Lum-BC specimens: -fresh (~40), for culturing in vitro (Patient-Derived-Organoids,PDO) and in vivo/mice (Patient-Derived-Xenografts,PDX); -frozen from young (~50) and non-young patients (~50) for NGS analyses; -FFPE young (120) for validation.
Results: A generated living biobank of Lum-BCYW-derived-PDX and -PDO, represents a model to study Lum-BCYW. Preliminary data confirm that Pi3K and p53 pathways mutations are enriched in Lum-BCYW, hence NGS on 28-genes Illumina-panel, custom-prepared was used to identify other genetic fingerprints of Lum-BCYW. Bioinformatic analysis is ongoing to identify mutation-enriched genes, drivers of aggressiveness, to be validated in Lum-BCYW-PDOs and -PDXs, transferable to clinical practice.
Conclusion: Thanks to the efforts of a multidisciplinary team and the generation of models, our results could provide tailored solutions, improving our understanding of BCYW biology and patients' outcome.

PS-01-028

Molecular subtypes of breast cancer: Long-term incidence trends and prognostic differences

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Objective: Temporal changes in incidence and prognosis of molecular breast cancer subtypes are poorly described. We assessed long-term trends in a population of Norwegian women born 1886–1977.
Method: 52 949 women were followed for breast cancer occurrence, and 1423 tumours were reclassified into molecular subtypes using immunohistochemistry and in situ hybridization. We compared subtype-specific incidence rates among women born 1886–1928 and 1929–1977, and performed multiple imputations to account for cases of unknown subtype. Prognosis was compared for cases diagnosed before 1995 and in 1995 or later, estimating cumulative risk of death and hazard ratios (HR).
Results: For women aged 50–69 years, incidence rates of Luminal A and Luminal B (HER2-) were higher among women born in 1929 or later, compared to before 1929 (IRRs 50–54 years, after imputations: 3.5, 95 % CI 1.8–6.9 and 2.5, 95 % CI 1.2–5.2, respectively). Prognosis was better for women diagnosed in 1995 or later, compared to before 1995 for Luminal A (HR 0.4, 95 % CI 0.3–0.5), Luminal B (HER2-) (HR 0.5, 95 % CI 0.3–0.7), and Basal phenotype (HR 0.4, 95 % CI 0.2–0.9).
Conclusion: We found a clear secular incidence increase for Luminal A and Luminal B (HER2-) subtypes, combined with improved prognosis for these subtypes and the Basal phenotype.

PS-01-029

Stromal tumour lymphocyte infiltration as a prognostic tool in triple negative breast cancer

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Objective: Stromal tumour infiltrating lymphocytes (sTILs) have been proposed as a potential tumour biomarker in triple negative breast cancers (TNBC).We aimed to examine the association between sTILs and clinicopathological parameters and outcome in TNBC.
Method: We evaluated sTILs in 303 TNBCs using the TILs International Working Group Guidelines. Lymphocyte-high (LHBC) and Lymphocyte-predominant breast cancer (LPBC) were defined as sTILs ≥25 % and ≥50 % respectively. The prognostic significance of sTILs in 10 % increments, of LHBC and of LPBC was determined.
Results: The median sTIL count was 15 % (range:0–90 %; mean:22 %). LHBC was significantly associated with histological type, poorly-differentiated tumours, and high nuclear grade ($p = <0.001$,$p = 0.047$,$p = 0.029$). On multivariate analaysis, the magnitude of the sTILs effect on disease-free-survival (DFS) was most significant with >25 % cut-off (LHBC) (HR = 0.44, 95%CI: 0.25–0.79, $p = 0.007$). Its impact on overall-survival (OS) was still significant (HR = 0.56, 95%CI = 0.32–0.99, $p = 0.047$). The association between LPBC (sTILs > 50 %) and DFS or OS was not significant on multivariate analysis (HR = 0.48, 95%CI = 0.22–1.06, $p = 0.07$; HR = 0.59, 95%CI = 0.28–1.23, $p = 0.162$ respectively).
Conclusion: Our findings support a prognostic role for sTILs in TNBC. sTIL-high (>25 %) was an independent predictor of survival. The lack of prognostic significance of LPBC may be due to the small numbers in this category.

PS-01-030

G-protein coupled estrogen receptor 30 (GPR30) expression in breast carcinoma

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Objective: GPR30 , seven transmembrane-G protein coupled receptor is known for its ability to bind estrogen and relay rapid intracellular signals leading to activation of estrogen receptor kinase (Erk), culminating in heparin bound-epidermal growth factor (HB-EGF) ectodomain shedding in breast cancer cells. In this study we investigated the possible association between GPR30 expression with molecular and clinico-pathological parameters.
Method: We studied the expression of GPR 30 in 65 cases of breast carcinoma diagnosed and treated at NEIGRIHMS, Shillong, India between the period 2010 to 2015.The study was approved by Institute's Ethics Committee.
Results: H score for GPR 30 of 100 or more in 44 cases (67.6 %)was considered as positive expression. Co-expression of GPR30 with ER was seen in 50 % of cases whereas 17 % expressed only GPR30. Significant correlation was seen with estrogen receptor (ER) & progesterone receptor (PR) status of the tumour with p value of 0.048 and 0.028 respectively.
Conclusion: This study indicates that GPR 30 does not depend on ER. GPR positive tumours represent a new subset and possible therapeutic target that may complement the current modes of treating breast cancers.

PS-01-031

An uncommon beta catenin gene deletion in a breast desmoid-type fibromatosis

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Objective: Desmoid-type fibromatosis (DTF) has a peculiar high frequency of mutations in exon 3 codons 41 and 45 of beta catenin gene (CTNNB1). Other CTNNB1 mutations are rare in DTF. Our objective is to describe one of such unusual mutation.
Method: A 21 years-old female patient, HIV positive by vertical transmission, with undetectable viral load, was under surveillance for breast nodules, when a new nodule was detected 5 months prior to surgery, described as an irregularly shaped 3.1 cm nodule with spiculated margins by ultrasound, in the junction of inner quadrants of her left breast.
Results: The tumour was resected and a final diagnosis of DTF was done, with nuclear beta catenin immunohistochemical staining and focal smooth muscle actin positivity. Cytokeratin 5, p63, S100, epithelial membrane antigen, desmin, CD117 and CD34 were negative. Sanger sequencing of CTNNB1 exon 3 disclosed a 30 bases in-frame deletion, A39-G48del.
Conclusion: CTNNB1 mutations outside the typical point mutations in codons 41 and 45, as illustrated in this case, are extending the range of possible activating CTNNB1 mutations seen in DFF. We describe a rare exon 3 CTNNB1 deletion for the first time in an extra-abdominal desmoid-type fibromatosis, only once previously described in an intra-abdominal case.

PS-01-032

New prognostic integrated pathological index in breast cancer patients

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Objective: Histopathological features of breast cancer are the basis for the pathological report, it usually contains all the necessary information to make decisions with respect to prognosis and treatment. The best way to improve the informative value of pathological reports is the unification of the results using semi-quantitative assessment methods. The purpose of the study was to assess the prognostic power of integral pathological index with the respect to five-year overall survival rates (OS) of breast cancer patients.

Method: A retrospective study of 128 breast tumour samples of patients treated in Regional Oncology Center (Ulyanovsk) and Research Center for Obstetrics, Gynecology and Perinatology (Moscow). New Ulyanovsk prognostic integral index (UPI) based on the use of semi-quantitative assessment of the total six main micromorphological features that characterize carcinomas: degree of cellular differentiation, cellular polymorphism, mitotic activity, growth pattern, lymphovascular invasion, stromal reaction. According to the total score all breast carcinomas were divided into four groups: carcinomas of very low (UPI scores of 4–6), low (7–10), moderate (11–15) and high malignant potential (16–20).
Results: A statistically significant correlation between 5-year overall survival of breast cancer patients and UPI total score was obtained. The lower grade of malignancy was associated with the better long-term prognosis. In the group of very low malignant potential 5-year OS was 100 % vs 32 % 5 in group of high malignant potential ($p < 0.01$).
Conclusion: Statistically significant correlation between UPI and 5-year OS allows to expect that this new semi-quantitative would be used in the practice of pathologists for unified pathological assessment and helpful for clinicians in adjuvant treatment planning.

PS-01-033
Pathological predictors of axillary lymph node metastases in women with breast cancer
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Objective: The purpose of the study was to assess the impact of different clinical and pathological factors on axillary lymph node involvement in breast cancer patients.
Method: A retrospective study of 530 breast cancer patients treated in Regional Oncology Center (Ulyanovsk) and Research Center for Obstetrics, Gynecology and Perinatology (Moscow). All the patients received surgery including axillary lymph node dissection. Pathological factors evaluated were: traditional pathological criteria (primary tumour size, histological variant, grade, HR- and Her-2/neu status) and total pathological index (Ulyanovsk prognostic index). Ulyanovsk prognostic index (UPI) is total score of six main pathological criteria that characterize the malignancy of epithelial tumours: degree of cellular differentiation, cellular polymorphism, mitotic activity, growth pattern, lymphovascular invasion, stromal reaction.
Results: Of the total 530 breast cancer patients 257 (48.6 %) found to be node positive. Univariative regression analysis revealed tumour size ($p = 0.00006$), tumour grade (0.0025), Her-2/neu status ($p = 0.02$) and UPI ($p < 0.0000001$) to be the most powerful predictors of axillary lymph node involvement. Tumour histology ($p = 0.204$), ER status ($p = 0.56$), RP status ($p = 0.75$), had no statistically significant association with axillary lymph node metastases.
Conclusion: Tumour size, grade, Her-2/neu status and Ulyanovsk prognostic index are independent prognostic factors for axillary lymph node involvement in general population of breast cancer patients. Ulyanovsk prognostic index has the highest predictive value and helps to define malignant potential in each particular case.

PS-01-034
Percentage of Her2 positive cells in immunohistochemistry-equivocal (2+) invasive breast cancer and its significance as a predictive value for the amplification status
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Objective: We analyzed Her2 amplification status in breast cancer with equivocal immunohistochemistry results to investigate the relation between the percentage of positive cells and the amplification status.

Method: We retrospectively studied 150 breast cancers with equivocal immunohistochemical staining (2+ score according to 2013 ASCO/CAP guidelines) selected from a total of 1206 cases. The percentage of Her2 positive tumour cells were categorized into three groups: <20 %, 20–40 %, >40 %. Moreover, we analyzed the proliferation index (Ki-67) using a 20 % cut-off between low and high proliferation index.
Results: Her2 fluorescence in situ hybridization (FISH) was performed in all cases scored 2+. 38 cases (25,5 %) were amplified; 1 (2 %) in the <20 % group, 7 (18 %) in the 20–40 % and 30 (80 %) in the >40 %. Ki-67 was higher than 20 % in 16 cases (53,3 %) from the >40 % group.
Conclusion: A high percentage (>40 %) of positive cells predicted Her2 amplification, especially when in association with high Ki-67 index. We suggest to repeat FISH test in non-amplified cases with >40 % of positive cells and in amplified cases with <20 % of positive cells. Furthermore, we believe that the evaluation of positive cells percentage and its correlation with the amplification status could represent an important internal laboratory quality control.

PS-01-035
Tumour-infiltrating lymphocytes and stromal reaction in male breast cancer
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Objective: Aim of this study was to analyze pathological characteristics of MBC (size, histological type, histological grade, in situ component, lymphovascular invasion, perineural invasion, necrosis, microcalcifications), with special interest in tumour-infiltrating lymphocytes and stromal reaction.
Method: This retrospective study involved 31 patients that were surgically treated in Oncology Institute of Vojvodina, from January 1 st 2007 till March 31 st 2017.
Results: The average age of patients was 65.1 ± 10.2 years. The most common histological subtype was invasive carcinoma not otherwise specified (NOS) in 90.3 % of patients ($N = 2$), while the most common molecular subtype was the luminal A, in 70.9 % of subjects ($N = 22$). In most cases, 61.3 % ($N = 19$), cancers were intermediate histological grade (HG2), with median of Nottingham score of 6. Primary tumour size was 27.2 ± 14.9 mm at the time of surgery, with 51.6 % ($N = 16$) being pT2 stage. Chi-square test, Fisher's exact test and Kruskal-Wallis H test showed no significant differences or correlations between molecular and histological subtypes, and pathohistological characteristics in analyzed specimens. There was statistically significant medium positive correlation between size of primary tumour and tumour-infiltrating lymphocytes ($r = 0.42$, $p = 0.018$), as well as between size of primary tumour and stromal reaction ($r = 0.41$, $p = 0.022$). Stromal reaction was also positively correlated with lymphovascular invasion ($r = 0.37$, $p = 0.041$).
Conclusion: Even though the incidence of breast cancer in men is low, it is still rather unknown biological entity that might require different approach in diagnostics, staging and therapy compared to that of women.

PS-01-036
Immunohistochemical expression of epidermal growth factor receptors, estrogen receptors beta, androgen receptors, MLH1, MSH6, PMS2, and MSH2 proteins in triple negative breast carcinoma
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Objective: To compare the immunohistochemical expression of epidermal growth factor receptors (EGFR), estrogen receptors beta (ER-β), androgen receptors (AR), MLH1, MSH6, PMS2 and MSH2 proteins in tumour cells of the triple negative breast cancer and other breast cancers.

Method: The study was conducted on 30 samples of tumour tissue of patients diagnosed with triple negative breast cancer and 30 samples of tumour tissue of other breast cancers. Immunohistochemical expressions of EGFR, ER-β, AR, and MLH1, MSH6, PMS2, and MSH2 proteins were assessed semiquantitatively as 0 (negative), 1+ (up to 10 % positive tumour cells), 2+ (11 %–30 % positive tumour cells), 3+ (31 % and more positive tumour cells). Relations with patients' age, tumour size, differentiation, HER2 amplification, Ki-67, and axillary lymph node status were calculated.
Results: IHC expressions in the triple negative breast carcinoma group were: EGFR 36,7 %, ER-β 100 %, AR 43,3 %, MLH1 100 %, MSH6 100 %, PMS2 100 %, and MSH2 proteins 100 %. There were no significant differences compared to the control group IHC expressions nor to the most other analyzed parameters. The lower the degree of the tumour differentiation/the higher the percentage of Ki-67 positive tumour cells, the rarer the expression of AR in tumour tissue is ($p < 0{,}001$). The expression of the MSH6 protein is associated with a significantly higher percentage of Ki-67 positive cells ($p = 0.001$). The lower the degree of tumour differentiation, the higher is the expression of MSH6 ($p = 0.002$).
Conclusion: Triple negative breast carcinoma tissue positivity to the EGFR, ER-β, and AR points to a possible targets of hormonal or other aimed therapy in this group of breast cancer.

PS-01-037
Epithelial mesenchymal transition (EMT) phenotype in metastatic and non-metastatic breast cancer
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Objective: Breast cancer (BC) in Oman affects younger women with a more aggressive course. Clinico-biological variables predict disease aggression but metastasis prediction is unreliable. Epithelial-mesenchymal transition (EMT)/ cancer stem cell (CSC) phenotype may predict metastatic potential. Its association with conventional clinico-pathological predictors in metastatic breast cancer was studied.
Method: In 96 women with breast cancer, the association of age, pregnancy/lactation, TNM stage, tumour type, grade, ductal carcinoma in situ (DCIS), lymphovascular invasion (LVI), receptor expression, Ki67 proliferation index (Ki67 PI) was correlated with EMT/ CSC phenotype and metastasis. EMT phenotype was established by expression/ loss, of two or more markers including vimentin, beta-catenin, e-cadherin, n-cadherin, smooth muscle actin, fibronectin and stromelysin-3 and CSC phenotype by CD44+/CD24-/low phenotype.
Results: Young age, LVI and EMT phenotype had a strong association with metastasis; CSC phenotypic expression approached significance. Vimentin, fibronectin and MMP-11 were reliable markers of EMT; dual EMT and CSC phenotype (Vim+/ CD44+/ CD 24-/low) seen in apocrine variant, basal-like tumours and triple negative cancers. EMT phenotype had a strong association with Ki67 proliferation index (PI); CSC with HER2-like tumours and distant metastasis.
Conclusion: This study's significance lies in its application of EMT signature to clinical biopsies to predict metastatic potential.

PS-01-038
Does progesterone receptor loss identifies two distinct Luminal A breast cancer subgroups in male
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Objective: In this study, we aim to get a deeper insight into the prognostic significance of progesterone receptor loss in luminal A breast cancer subtype in male.
Method: A total of 73 cases of male breast cancer (MBC) with accessible FFPE material and outcome data were investigated. We evaluated four subgroups within the Luminal A subtype according to HER2 expression and PR status.
Results: Among the 73 cases, 29 (39.7 %) were of Luminal A subtype. The ER+/PR+/HER2− subgroup was the most common (32.9 % of Luminal A); it was the one with the lowest rate of distant metastasis as well as with the best overall survival (OS) when compared with the other Luminal A subgroup. No cases of the ER+/PR−/HER2+ subgroup were identified. On the contrary, the ER+/PR-/HER- subgroup was the one that showed the worst OS and the highest rate of distant metastasis when compared with the other Luminal A subgroups but this difference wasn't statistically significant ($p = 0.08$).
Conclusion: In conclusion, after dividing the Luminal A subtype group into four subgroups according to PR and HER2 status, we provided evidence of a relatively good prognosis of the ER+/PR+/HER2− subgroup, and confirmed the significant impact of progesterone receptor status on the outcome of MBC patients.

PS-01-039
Do tumour characteristics of primary breast carcinoma determine status of sentinel lymph nodes?
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Objective: The purpose of this study was to compare sentinel (SLN) and axillary lymph nodes (ALN) status with primary tumour characteristics.
Method: This retrospective study included 714 women diagnosed with invasive breast cancer at the University Medical Centre Maribor, Slovenia. All patients underwent SLN biopsy followed by ALN dissection in case of positive SLN. Tumour type, size, grade, stage, hormone receptor status, and HER2 status were recorded.
Results: Out of 714 patients, 269 had positive SLN. In144 SLN we found macrometastases (MMT), in 80 micrometastases (MIT) and in 45 isolated tumour cells (ITC). Of 269 SLN positives, 58 patients had positive ALN. Tumour stage was associated with MMT ($p = 0.039$), but not with ITC. Tumour grade 1 correlated with MMT ($p = 0.026$) and MIT ($p = 0.013$) only. The risk of finding metastases in ALN differs significantly for MMT ($p = 0.001$), but not for MIT ($p = 0.817$) or ITC ($p = 0.097$). In cohort of 58 patients with positive SLN and positive ALN, tumour size was <2 cm in 31.0 % and ≥2 cm in 69.0 %.
Conclusion: Our preliminary study indicates the association of tumour stage and tumour grade with status of SLN. Compared to MIT and ITC, MMT in SLN represent a higher risk to invade other axillary lymph nodes.

PS-01-040
Epidemiology of breast cancer in Newfoundland, Canada: Post-Cameron inquiry analysis
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Objective: The objective of this study was to examine the epidemiological characteristics of breast cancer population in Newfoundland, Canada, post-Cameron Inquiry.
Method: This is a population-based study examining all breast cancer patients tested for hormone receptors (HR) in Newfoundland during the first 6 months of recommencing testing at the central immunohistochemical (IHC) laboratory (post Cameron inquiry). Clinicopathologic data was collected using the laboratory information system.
Results: A total of 662 patients with breast cancers, mean age (±SD) of 61.3 (±12.9) years, are identified. Median fixation time was 48 hrs. Eighty-five percent of breast cancers were invasive ductal carcinoma (NOS), followed by invasive lobular carcinoma (7 %) and other types.

80.2 , 69.9 and 15.9 % of breast cancers were ER, PR and Her2 positive. 10.2 % of equivocal Her2 (IHC) was subsequently negative using FISH analysis. A significant statistical association between high- grade tumours and negative ER and PR immunostains was found ($P < 0.0001$). Positive Her2 immunostains were also associated with high-grade tumours ($P < 0.0001$).

Conclusion: A significant improvement in breast surgical pathology practices was observed in the post-Cameron inquiry era. The epidemiologic data on breast cancer in Newfoundland is consistent with other North American jurisdictions. Incorporating and analyzing clinicopathologic information along with IHC Quality Assurance measures can further enhance breast cancer pathology practices in Newfoundland.

PS-01-041

Encysted papillary carcinoma of the breast with macrometastasis

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Objective: Encysted papillary carcinomas are currently classified within the in situ range of lesions. We present a case of encysted papillary carcinomas with lymph node macrometastasis. This cases raises the question, are encysted papillary carcinomas truly an in situ lesion?

Method: A 70 year old female presented with a 6 month history of a progressively enlarging cystic mass in the right breast. Mammogram and ultrasound showed a 120 mm mass with normal axilla. An encysted papillary carcinoma was reported on core biopsy, followed by a wide local excision and sentinel node biopsy.

Results: In the excision specimen the cystic mass measured 110 mm in maximum dimension. Scattered solid polypoidal areas were noted, the largest measuring 20 mm. Two sentinel lymph nodes were excised. Histologically the tumour was an encysted papillary carcinoma of predominately intermediate nuclear pleomorphic grade. Mitoses were abundant. There was no evidence of conventional invasion. Unexpected for these types of breast carcinomas, one of the sentinel lymph nodes contained a macrometastasis (12 mm) of encysted papillary carcinoma. Immunohistochemical staining of the tumour and macrometastasis in the axillary lymph node was positive for oestrogen and progesterone receptors, and HER-2 negative.

Conclusion: Encysted papillary carcinomas are staged as pTis. In this case that is despite the presence of a lymph node macrometastasis (pN(mi)). We believe this is the first case describing lymph node macrometastatic disease in such lesions. There are no clear guidelines on how to stage or manage these lesions. Post follow up by breast MRI showed no other lesions in the breast and she recently had an axillary node clearance, of which the results are awaited.

PS-01-043

Invasive breast carcinomas with peritumoural PASH-like stroma show lower level of CD68(+) tumour associated macrophages than those of invasive carcinomas without peritumoural PASH-Like Stroma (PASH: Pseudoangiomatous Stromal Hyperplasia)

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Objective: The significance of association between cancer and its stromal microenvironment has been recognized. We aimed to investigate the immunohistochemical staining features of D2-40 (podoplanin), SMA (smooth muscle actin) and CD68 (pan-macrophage marker) in patients with early stage invasive breast cancer with/out peritumoural PASH-like stroma.

Method: The H&E sections of core needle biopsy specimens of invasive breast carcinomas diagnosed during 1-year time period were reviewed in terms of the presence of accompanying PASH-like stroma retrospectively. Cases with similar pattern of growth in their surgical excision materials were included. Eight cases were grouped as 'Invasive tumour with PASH-like stroma' and 21 cases as 'Invasive tumour without PASH-like stroma', consecutively. The results of immunohistochemical staining for D2-40, SMA and CD68 were noted semiquantitatively as 'negative','weak', 'moderate' or 'strong'.

Results: CD68 was found significantly lower ($p < 0{,}000...$) in invasive tumour with peritumoural PASH-like stroma than those of tumour without PASH-like stroma. No significant differences were found for SMA and D2-40 between two groups.

Conclusion: Tumour-associated macrophages (CD68 positive) in tumour stroma have been demonstrated in association with tumour behavior in several studies. The presence of peritumoural PASH-like stroma, which is poorly staining for CD68, might be a morphological clue for the behavior of tumour.

PS-01-044

Histopathology of transgender breast specimens: Expect the unexpected!

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Objective: This study examined the histopathological features in resection specimens after bilateral mastectomy in a female-to-male transgender population.

Method: Haematoxylin/eosin stained sections of 148 bilateral mastectomy specimens were retrieved from the Department of Pathology of Ghent University Hospital (Ghent, Belgium). The presence of the following lesions was assessed by two pathologists: apocrine metaplasia, lactational changes, columnar cell changes, sclerosing adenosis, fibroadenoma, usual ductal hyperplasia (UDH), flat epithelial atypia (FEA), atypical ductal hyperplasia (ADH), ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS) and invasive breast cancer. In addition, the stroma/fat ratio and the amount of lobules per 10 low-power fields (LPF; 40× magnification) were investigated.

Results: Eighty percent of the breasts showed a stroma/fat ratio higher than 3/1. Apocrine metaplasia was seen in 23.6 %, lactational changes in 2 %, columnar cell changes in 37.2 %, sclerosing adenosis in 4.7 %, fibroadenoma in 4.1 %, UDH in 27 %, FEA in 0.7 % and ADH in 3.4 %. LCIS and invasive lobular carcinoma were not observed. One 31-year-old patient showed DCIS and invasive ductal carcinoma.

Conclusion: Although invasive cancer is a rare finding, careful routine histopathological examination of resection specimens after bilateral mastectomy in female-to-male transgenders remains important. Results from an extended cohort are pending.

PS-01-045

Clinicopathologic factors associated with HER2 gene amplification in invasive breast carcinomas with equivocal HER2 immunostaining: Experience from a single institution

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Objective: The assessment of HER2 status by FISH in breast carcinomas with equivocal immunostaining (HER2 IHC 2+) has become a routine practice for therapeutic purposes. Our aim was to assess clininopathologic factors associated with HER2 amplification by FISH in breast invasive carcinoma with HER2 IHC 2 + .

Method: It was a retrospective study of 87 cases of primary breast carcinomas with equivocal HER2 IHC 2+, that underwent FISH asssessment

for HER2 amplification (2009–2016). IHC and FISH were reported according to ASCO/ACP 2008 and 2013 guidelines.
Results: The mean age was 49 years. At IHC, estrogen receptor (ER) was positive in 65/74 cases (87.83 %), progesterone receptor (PR) was positive in 82.43 %, Ki-67 ≥ 20 % in 87.5 %. The overall HER2 amplification rate was 25.28 % (22 cases) with an increase according to the 2013 ASCO/ACP guidelines (26.66 % vs 23.80 %). There was no correlation between HER2 amplification and age or tumour grade ($p > 0.05$). ER negativity was associated with HER2 amplification ($p = 0.02$).
Conclusion: A substantial proportion of breast carcinomas with equivocal HER2 immunostaining harbor gene amplification, with significant correlation with ER negativity. The new ASCO/ACP guidelines has led to a slight increase in HER2 amplification rate.

PS-01-046
Outcome impact of PIK3CA mutations in HER2-positive breast cancer patients treated with neoadjuvant chemotherapy: Sequential analysis
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Objective: We investigated the association between PIK3CA mutations and outcome of neoadjuvant chemotherapy(NAC) in human epidermal growth factor receptor 2(HER2)-positive breast cancers.
Method: Total 100 HER2-positive breast cancer patients who undergone NAC and surgery in Samsung Medical Center between 2004 and 2016 were included. PIC3CA mutation was sequentially assessed in pre-NAC, post-NAC and recurrent specimen, if present.
Results: In sequential specimen of 17 patients(17 %), PIC3CA mutations were identified, and mutant group showed shorter disease-free survival(DFS) than wild group (41.48 months vs 115.06 months; $p = 0.022$), but pathologic complete remission(pCR) didn't show a significant difference. On multivariate analysis, PIC3CA mutation was significant factor for faster tumour recurrence. (B = −1.304; 95 % CI 0.079–0.932; $p = 0.038$). In pre-NAC specimens, there was no difference in pCR between PIK3CA wild and mutant type. But in post-NAC specimens, PIK3CA mutant type was correlated with lower pCR compared with wild type and uninvestigated group. (0 % vs 24.3 % vs 26.3 %, $p < 0.001$)
Conclusion: PIC3CA mutation in HER2-positive breast cancer showed lower pCR and shorter DFS than wild type in HER2-positive breast cancer patients. PIC3CA mutation may be a biomarker for NAC in HER2-positive breast cancer.

PS-01-047
Impact of crystal analyser-based phase contrast X-ray computed tomography on histopathology
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Objective: This review provides an overview of emerging X-ray phase contrast imaging techniques incorporating X-ray dark-field imaging (XDFI), which has been developed over the past 15 years.
Method: The new imaging techniques use phase contrast rather than conventional absorption. The optical chain of XDFI consists of an asymmetrically cut, Bragg-type monochromator-collimator that provides a planar monochromatic X-ray beam which passes through the specimen mounted on a precision positioning stage; the X-ray beam exiting the specimen is split into dark and bright field images by a Laue-case angle analyser. High-resolution cameras are used to capture these images for further processing and tomographic reconstruction.
Results: The unique features of XDFI are its extremely high contrast (approximately 100:1 compared to absorption) and high resolution (10 to 20 microns). So far, we have shown that XDFI can provide images equivalent to the low to medium power light microscopes. XDFI-computed tomography (XDFI-CT) is also effective for three-dimensional rendering of anatomical structures such as breast lobules, the three layers of arteries, and articular cartilage; these features are barely visible in conventional absorption-based images. XDFI of breast tissue can discriminate between normal tissue, diseased terminal duct lobular units such as those present in cases of pure adenosis, and the involvement of lobular carcinoma in situ. By visualizing the mammary ducts and basement membrane integrity, it can also differentiate between invasive and in situ cancer.
Conclusion: XDFI opens a new window on histopathologic details of unstained, minimally-prepared pathology specimens. Although further clinicopathological validation is necessary, this new technology shifts the boundaries between radiology and pathology.

PS-01-048
Link between cancer stem cells and p53 expression in breast cancer tissue
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Objective: As recently shown, p53 plays an important role in stem cells. The aim of this research was to find a link between p53 and cancer stem cells (CSC) in breast cancer.
Method: 120 cases of breast cancer were explored. In all cases expression of ALDH1A1 (for detection of CSCs), p53, ER, PR, HER-2/neu, and Ki-67 was examined. Immunohistochemical method was applied. All cases were divided into two groups—with presence ad absence of CSCs in cancer pool. The first group contained 20 cases with 2+ and 3+ ALDH1A1 expression, the second—100 cases with 0 and 1+ ALDH1A1 expression. All cases were divided to immunohistochemical subtypes.
Results: The average level of p53 expression of both groups of ALDH1A1 expression was almost the same (3.2 ± 0.5 and 2.7 ± 0.3 respectively, $p > 0.05$). But in triple negative subtype the expression of p53 was higher in the group with absence of CSCs (6.1 ± 1.5 vs 4.6 ± 0.8, $p < 0.05$). In HER-2 positive subtypes (HER-2 overexpression and Luminal B) the expression of p53 was higher in the group with presence of CSCs (5.5 ± 1.7 and 4.3 ± 1.1 vs 3.8 ± 0.5 and 1.95 ± 0.7 respectively, $p < 0.05$).
Conclusion: Expression of p53 links to presence of CSCs in cancer pool as well as receptor status of breast cancer.

PS-01-049
Cutaneous metastases of breast cancer: A study of telve cases
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Objective: Metastases of breast cancer to the skin are not rare, but sometimes they can clinically mimic other skin diseases. We present 12 cases with diverse natural history.
Method: All cases were retrieved from the pathology files of Papageorgiou Hospital between 2011 and 2016. Eleven patients were female with a mean age of 63 years (range 41–83 years). The sole male patient was 66 years old and the skin metastasis preceded the diagnosis of the primary tumour. Tissue sections of skin biopsies were stained for a standard antibodies panel (Cytokeratin 7, ER, PgR and HER 2).
Results: Four female patients had an invasive lobular carcinoma and 7 an invasive ductal carcinoma. Skin metastasis occurred in a range of 4–

20 years (mean time 9 years) after the initial diagnosis. All patients had already a history of blood-borne metastases (in bones, lung, liver and brain). All cases except two were ER and PgR positive and HER 2 negative. In one case the tumour was triple negative. Three female patients died 1–3 years after the detection of skin metastasis.
Conclusion: Carcinomas of the breast rarely become clinically evident through skin metastasis. Immunohistochemistry is helpful if there is no previous history. Skin metastasis is usually a long-term event following diagnosis and an expression of tumour progression.

PS-01-050
Metastases from unusual primaries to the breast: Report of two cases
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Objective: Metastases from extramammary primaries account for 0,2–1,3 % of all breast cancers. Melanoma and mucinous colon cancer metastatic to breast are extremely rare
Method: The first case corresponds to a 63-year old female patient, who was diagnosed with primary colon mucinous adenocarcinoma. Breast MRI demonstrated a mass at the 10–11 o'clock region of the right breast. We also present a case of a 69-year old female patient, who was diagnosed with nodular melanoma. Mammography confirmed a lesion at the 3 o'clock region of the left breast
Results: The first patient underwent core needle biopsy, which revealed a poorly differentiated adenocarcinoma. The tumour was positive for CK20, CDX2 and negative for ER, PR, cerbB2 and CK7. The second patient underwent partial mastectomy. Microscopic examination revealed a tumour (measuring 2,2 cm) which consisted of epithelioid cells with mild pleomorphic nuclei. The malignant cells were positive for Melan A, HMB45 and S100 and negative for KerAE1/AE3
Conclusion: Careful examination of the morphology of the malignant cells, and an accurate clinical history are required for a proper diagnosis and a proper treatment plan

PS-01-051
Examination of tumour infiltrating lymphocytes in breast cancer
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Objective: Several studies consider the prognostic value of tumour infiltrating lymphocytes (TILs) in breast carcinomas (BC). We analysed stromal TIL on Haematoxylin and Eosin (HE) stained slides of surgically resected BC tissues and correlated TIL ratios with subtype and patients' follow-up data.
Method: 78 LUMA, 94 LUMB1, 48 LUMB2, 49 HER2+ and 52 TNBC breast carcinomas diagnosed between 2000 and 2009 with known follow-up data were analysed. Stromal TIL was evaluated at 200× magnification based on the recommendations of the International TILs working group (2014). Distant metastasis free survival (DMFS) was recorded in all cases. Statistical analysis was performed with SPSS Statistics for Windows, Version 22.0.
Results: Reliable follow-up data were available in 307 cases. Distant metastases (DM) was detected in 80/307 (26,1 %) cases. Significantly higher TIL ratio was observed in hormone receptore-negative (HR-negative) BC subgroups compared to HR-positive groups ($p < 0.001$), and high TIL ratio was also significantly inversely associated with DM formation ($p = 0.011$). Fifty of 225 cases (22.2 %) without metastasis presented high (≥10 %) TIL content. In metastatic group this ratio was 12.5 %.
Conclusion: TIL is a promising prognostic marker in at least HR-negative BC. High TIL ratio may have a role in preventing metastatic spread in a fraction of BC cases.

PS-01-052
Association between stromal tumour lymphocyte infiltration in the needle core biopsies and paired post-neoadjuvant chemotherapy resection specimens in triple negative breast cancer
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Objective: Stromal tumour infiltrating lymphocytes (sTIL) are prognostically important in triple negative breast cancer (TNBC). Neoadjuvant chemotherapy (NACT) is now the standard of care for TNBC; and the effect of NACT on the sTIL population and its potential prognostic significance is unknown. Our aim was to investigate the association between sTILs in the pre-treatment needle core biopsy (NCB) and the therapeutic excision specimen post-NACT for those who have post NACT residual disease.
Method: sTILs were assessed, using the International Working Group Guidelines, on 26 paired pre-treatment NCB and post-NACT therapeutic excision (THE) specimens with residual disease.
Results: The median sTIL count was the same in pre-treatment NCBs and post treatment specimens (10 %) with no significant difference in the mean sTILs (mean = 15.25 and 18.77 % respectively,$p = 0.317$: paired t-test). The differences in the absolute sTILs values between the paired NCB and THE were low (range:0–45 %; median:5 %; mean;11.31 %). There was a strong correlation between sTILs values in NCB and THE specimen ($R = 0.67$;$p = 0.002$). The explained variance (R2) showed that 45 % of the excision results for sTILs can be predicted by the NCB results.
Conclusion: NACT had no significant effect on sTIL counts when residual disease remained post-treatment. sTILs counts in NCBs are representative of sTILs in the larger specimen

PS-01-056
Adenomyoepithelioma of the breast with atypical lobular hyperplasia
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Objective: Adenomyoepithelioma (AME) of the breast is a rare tumour with biphasic neoplastic proliferation of glandular and myoepithelial cells. AME is frequently regarded as a benign tumour, but local recurrence or malignant transformation have been reported. The association of AME with lobular neoplasia is very rare, with only one previously reported case in the literature.
Method: A 42-year-old female presented with a solid mass in her right breast. Core needle biopsy of the lesion showed lobular neoplasm.
Results: In the serial sections of the excional biopsy, a solid, well-circumscribed, gray-white, firm nodule was observed. Histologically, the tumour had a biphasic nature, composed of cuboidal to columnar, epithelial-lined tubules surrounded by myoepithelial cells. In some areas, dyscohesive neoplastic cells were observed filling the glandular structures. Immunohistochemically, the myoepithelial cells were positive with p63 and smooth-muscle actin, and there was absence of e-cadherin expression in the dyscohesive groups. The lesion was diagnosed as AME with atypical lobular hyperplasia.
Conclusion: Due to the heterogeneity of the tumour, there may be diagnostic errors in needle biopsies. Detection of the structural pattern, biphasic cellular elements, and immunohistochemistry is significant in diagnosis. Although very rare, the identification of association with other neoplasms is important for adequate treatment.

PS-01-057
The accuracy of the preoperatively axillary ultrasound examination in predicting tumour parameters and the status of the sentinel lymph node involement in patients with breast carcinoma

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Objective: We aimed to evaluate the accuracy of preoperatively axillary ultrasound examination (US) in predicting parameters of the primary tumour and status of sentinel lymph node (SLN) involvement.
Method: We evaluated the axillary status of 54 patients preoperatively diagnosed with breast cancer on biopsy. We registered the USvLN lymph nodes (visible but not suspicious for malignancy) and measured the diameter and capsular thickness. These data were correlated with the pathological results of the surgical specimens. Patients with clinically and/or US suspicious lymph nodes were excluded.
Results: 35 cases (64 %) had axillary USvLN. Out of these, 15 (42 %) cases had positive and 20 (58 %) had negative SLN. Out of 19 cases in which the preoperatively US could not identify visible lymph nodes, 16 (84 %) had negative SLN and 3 cases had positive SLN. However, the USvLN cannot be correlated with positive SLN ($p = 0.06$). The diameter ($p = 0.73$) and cortical thickness ($p = 0.13$) cannot predict the positivity of SLN. Also, the USvLN cannot be correlated with the tumour diameter ($p = 0.15$), histological type ($p = 0.25$), grade ($p = 0.59$), molecular profile ($p = 0.09$). The accuracy of this investigation is 41 %.
Conclusion: The preoperatively US cannot predict the positivity of the axillary SLN. SLN biopsy cannot be avoided by using axillary US for staging.

PS-01-058
A case of multiple myeloma of the breast mimicking an inflammatory carcinoma
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Objective: We report a case of breast lesion, with clinical and radiological features of inflammatory carcinoma. It turns out to be the first symptom of Multiple Myeloma.
Method: A 92-year-old woman presented with a swelling on her left breast. Clinical examination revealed an erythematous and edematous breast. Mammography showed a large tumour with 16 cm. An ultrasound-guided core needle biopsy was performed.
Results: Histological examination shows extensive infiltration of biopsies by tightly packed immature cells with round cells with wide eosinophilic cytoplasm and prominent nucleoli. Immunohistochemistry revealed positivity for CD138, Kappa light chain, and negativity for Lamda light chain, CD56, Bcl-2, CD3, CD20, CD30, A1/A3 and Gata3. Ki-67 was positive in 100 %. These findings corroborated the diagnosis of plasmacytoma of the breast. An extensive search for multiple myeloma was performed and radiology revealed multiple masses throughout the skeletal system.
Conclusion: The involvement of breast by multiple myeloma has been rarely reported. Until now 21 cases have been described. Most frequent symptom is a palpable mass. When there is orange peel like texture of the skin, suggests inflammatory carcinoma. The differential diagnosis includes plasma cell mastitis, primary epithelial neoplasms of the breast, non-Hodgkin's lymphoma with plasmacytic features and epithelioid malignant melanoma.

PS-01-059
Histopathological findings contributing the differential diagnosis between primary breast carcinomas with neuroendocrine features (NEBC) and breast carcinomas suspicious for neuroendocrine features (Non-NEBC)
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Objective: We aimed to compare the morphological features of NEBC (positive for synoptophysin and/or chromogranin in ≥50 % of tumour cells) with non-NEBC (negative for synoptophysin and/or chromogranin).
Method: Structural patterns and cytological features of tumour cells were described on H&E sections in surgical excision materials, retrospectively. (NEBC = 25 cases, non-NEBC = 27 cases).
Results: The large-sized solid cohesive groups of tumour cells was determined in 3/4 of NEBC and 1/3 of Non-NEBC. Two thirds of non-NEBC group showed small/medium-sized solid cohesive groups of tumour cells accompanying with trabeculae, cords, glandular structures as well as single cells. Tumour cells with plasmocytoid, spindle and/or columnar shapes were mostly found in NEBC group. There was no difference in terms of the presence of signet ring cells, apocrine cells and extracellular mucin between two groups. While cytoplasmic features were noted as eosinophilic(%76) > foamy(%48) > clear(%12) in NEBC, it was eosinophilic(%66,6) > foamy(%63) > and clear(%41) in Non-NEBC. Peritumoural lymphocytic infiltration was seen in 2/3 of both groups. While the severity was mild in NEBC group, moderate in Non-NEBC.
Conclusion: The presence of large-sized solid cohesive groups, plasmocytoid, spindle and/or columnar shapes of tumour cells and mild peritumoural lymphocytic infiltration were mostly in favor of NEBC.

PS-01-061
Primary angiosarcoma of the breast in postmenopausal women: Case report
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Objective: Primary angiosarcoma of the breast accounts for 0.04 % of all breast malignant tumours.
Method: We present a 60-year-old female patient who came to our institution because of pain in the lumbar spine.
Results: Examination revealed a tumour of the right breast, the size of the child's head. The skin over the tumour was taut, mildly eroded with dampening. Using visualization radiological techniques (X-ray, ultrasound, CT scan), we diagnosed metastatic deposits in the liver, the lungs, the brain, in the vertebral body and ribs. Laboratory findings showed striking thrombocytopenia and anemia. Palliative mastectomy is done. In an operating material of the breast, we found a tumour node in size 14 × 10 × 11 cm, with an extensive area of central necrosis and bleeding. Positive immunohistochemical reaction is present on the endothelium-specific antibodies: CD31, CD34 and factor VIII, and negative on S100. The patient is indicated palliative therapy with bisphosphonates, supportive therapy and corticosteroid therapy because of poor general condition. Severe thrombocytopenia and anemia were refractory to the therapy applied. The patient dies 4 months after surgery.
Conclusion: Our patient is the fourth case of primary angiosarcoma of the breast in postmenopausal women in whom mastectomy were not performed, lymphedema was not evidenced or radiotherapy applied.

PS-01-062
Chondroid lipoma of the breast: A rare case report
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Objective: Chondroid lipomas are unique benign tumours and in breast tissue are considered extremely scarce. Chondroid matrix is rarely seen in benign conditions of human breast, so its presence raises a difficult differential diagnostic dilemma.

Method: We present the case of a 71-years-old woman who was found with a breast tumour, with imaging features of a lipoma in her left breast, during routine mammographic control, which was excised.
Results: Grossly, the tumour had 4 cm maximum diameter and was circumscribed with fatty consistency. Histologically, the tumour consisted of mature adipocytes admixed with nests of vacuolated lipoblasts and ovoid cells with granular eosinophilic cytoplasm and slightly pleomorphic nuclei, embedded in a prominent myxoid or hyalinized chondroid matrix. Mitoses or necrosis were absent. Immunohistochemically, the tumour cells expressed vimentin, CD34, CD68. S100 was detected in mature adipocytes. Accordingly, the diagnosis of chondroid lipoma was favored. The patient didnot receive further treatment and 2 years later has no evidence of tumour recurrence.
Conclusion: Chondroid lipoma of the breast is extremely rare and represents a challenging histological diagnosis due to its morphological similarity to myxoid liposarcoma and extraskeletical myxoid chondrosarcoma. The exact identification of this neoplasm cannot always be possible and it is based mostly on tumour's morphological features.

PS-01-063
Differential gene hypermethylation in breast cancer and non-tumoural tissue delineated by a 450 K methylation array
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Objective: To identify differentially methylated genes in breast cancer (BC) compared to non-neoplastic mammary tissue.
Method: Epigenome-wide DNA methylation profiling from 40 breast tumours and 6 non-neoplastic frozen cases was performed by an Illumina 450 K array (USA) after DNA extraction and bisulfite modification. Upon bioinformatics analyses, NKAPL, DLEU7 and PCDHA13 genes were selected for further validation by pyrosequencing in 50 breast tumours and 20 non-neoplastic tissues. Moreover, DLEU7 protein expression was explored by immunohistochemistry.
Results: We found 1867 hypermethylated and 15 hypomethylated probes recognizing CpG sites in promoter CpG islands (FDR < 0.05 and $\Delta\beta > 0.02$) from 733 and 9 hyper- and hypomethylated genes, respectively. NKAPL, DLEU7 and PCDHA13 genes showed higher methylation levels in breast tumours than in non-neoplastic tissue ($p < 0.05$). Interestingly, the adjacent-to-tumour tissue harboured intermediate levels of methylation. This epigenetic silencing was confirmed at the protein level for DLEU7. No association was found between these alterations and clinical variables.
Conclusion: This is the first description of the NKAPL, DLEU7 and PCDHA13 hypermethylation in BC, being already present in the adjacent-to-tumour tissue. DLEU7 is less expressed in tumour than in non-neoplastic tissue.

PS-01-064
Study of the prognostic role of immunohistochemical markers in a large series of breast cancer patients
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Objective: To evaluate the expression of immunohistochemical (IHC) markers in a series of breast tumours classified in pathological subtypes by St Gallen recommendations drawn in 2011 and 2013. The role of these proteins in disease-free survival (DFS) and overall survival (OS) was also assessed in the patients.
Method: A total of 647 tumours classified according to St Gallen 2011 recommendations were reclassified according to St Gallen 2013 into triple-negative breast cancer subtype (TNBC) and non-TNBC subtypes (luminal A-like, luminal B-like HER2-negative, luminal B-like HER2-positive, HER2-positive). IHC expression of androgen receptor, c-kit, cytokeratin-5/6, cytokeratin-17, E-cadherin, EGFR, p53, p63, p120 and vimentin was evaluated in tissue-microarrays, and their prognostic role was analysed in the non-metastatic BC patients ($n = 619$; median follow-up:7 years).
Results: Luminal B-like HER2-negative subtype incorporates patients of bad prognosis previously classified as the more indolent luminal A-like. P120 expression is a factor of good prognosis in non-TNBC patients (DFS: $p = 0.014$; OS: $p = 0.036$), whereas EGFR expression is a bad prognostic factor (DFS: $p = 0.001$; OS: $p = 0.004$).
Conclusion: The most recent St Gallen criteria are helpful for the pathologists to re-classify previous aggressive luminal-A tumours into the luminal B-like subtype. Additionally, p120 and EGFR are found to be new prognostic markers in non-TNBC patients.

PS-01-065
Clinicopathologic and immunohistochemical study of 21 cases of malignant papillary neoplasm of the breast
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Objective: To outline the clinicopathologic features of malignant papillary lesions of the breast and to distinguish them by morphologic features and immunohistochemical studies.
Method: Retrospective review of 21 cases of malignant papillary neoplasm of the breast between 2001 and 2016.
Results: The mean age of patients was 57.4 years. The mean size of tumours was 3,5 cm (1–9). There were 13 cases of invasive papillary carcinoma, 4 cases of encapsulated papillary carcinoma (including one with adjacent invasive carcinoma of no special type), 2 cases of solid papillary carcinoma, one case of intraductal papillary carcinoma and one papilloma with ductal carcinoma in situ. Immunostaining with myoepithelial markers, including Ck5/6 and p63 demonstrated the absence of myoepithelial cells both in the papillary fronds and at the periphery of the lesion in encapsulated papillary carcinoma. Hormonal receptors were positive in 6 cases of invasive papillary carcinoma and 3 cases of encapsulated papillary carcinoma.
Conclusion: The evaluation of papillary lesions remains a problematic area in breast pathology. Although many of them can be categorized based on examination of H&E-stained sections alone, others require the use of immunostains. Further studies are needed to elucidate the pathogenesis and the potential tools in stratifying these lesions.

PS-01-066
Expression of androgen receptors and c-kit (CD117) in triple-negative breast cancer
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Objective: A triple-negative breast cancer (tested negative for estrogen receptors, progesterone receptors and HER2) does not respond to hormonal or target HER2 receptor therapy and new medications are needed for effective treatment. For this purpose different tumour receptors were studied.
Method: We assessed immunohistochemically androgen receptors (AR) and C-Kit (CD117) in 110 cases of the triple-negative breast cancers (TNBC).

Results: Positive expression of AR >1 % was noted in 33 observations which was 30 % of the total number. 77 cases (70 %) were AR-negative. Average age of AR+ patients was older, than AR– (60 ± 13 years and 57 ± 12 years respectively). Histological degree of malignancy was higher in AR– tumours than in AR+. C-Kit positive expression (CD117) was registered in more than 1 % of cells in 46 cases (41.8 %). The mean age for C-Kit (CD117) positive tumours was significantly younger than for negative ones (54 ± 12 years and 61 ± 12 years, respectively). C-Kit (CD117) was defined in 29 cases (26 %) of Grade 3 tumours. In 10 cases overexpression was observed (9.1 %).
Conclusion: Thus, determination of androgen receptors and C-Kit (CD117) in breast cancer cells is a valuable immunohistochemical diagnostic method for subsequent selection of the target individual genomes and for TNBC immunotherapy.

PS-01-067
Syringomatous tumour of the nipple mimicking carcinoma. A case report
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Objective: We present a case of syringomatous tumour of the nipple (STN), a rare entity that can be misdiagnosed as malignancy.
Method: A 52-year-old female presented with discomfort and itching of her right nipple. On physical examination there was a firm right breast mass, accompanied by swelling of the overlying skin. On mammography, a subareolar density was seen. An initial dermal biopsy followed by complete excision of the nipple and part of the areola was performed.
Results: Microscopically, small, irregular glands with tear-drop or comma-shaped appearance were infiltrating among smooth muscle bundles and in perineural spaces. The tumour cells showed mild cytologic atypia. Immunohistochemically, the glands possessed a peripheral myoepithelial cell layer, positive for smooth muscle actin (SMA) and p63. Estrogen (ER) and progesterone (PR) receptors were negative. Mitoses, hemorrhage or necrosis were absent. STN was diagnosed.
Conclusion: The infiltrative growth of STN can be mistaken for tubular carcinoma. Positivity for SMA, negativity for ER and PR and epicenter of the lesion in the nipple rather than the breast are of diagnostic importance. STN is a tumour with potential for local recurrence but no metastatic behavior. Resection with wide margins is the recommended treatment.

PS-01-068
Primary neuroendocrine tumours of the breast: A retrospective study of 9 cases
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Objective: The aim of the study is to discuss clinico-pathologic features of primary neuroendocrine carcinomas of the breast.
Method: We report 9 cases diagnosed over a period of 11 years (2006–2017) at the university hospital of Sousse.
Results: The average age was 63.7 years (43–89 years). At the time of the diagnosis, tumours were classified T1 and T2 (8 cases), N1 (1 case) and M1 (1 case). The histological examination showed 4 cases of solid neuroendocrine carcinoma, 3 cases of large cell type and two cases of atypical carcinoid. All tumours were positive for chromogranin and 80 % of them were reactive for synaptophysin. Six tumours (60 %) were estrogen receptor-positive and 7 (70 %) progesterone receptor-positive. All tumours were negative for HER2/neu. All patients had surgical treatment with radical mastectomy in 7 cases. One patient had metastasis in the mediastinum. Adjuvant treatment was indicated according to histopronostic elements.
Conclusion: Primary neuroendocrine carcinoma of the breast is an unknown and rare pathologic entity due to its rare incidence and lack of definitive criteria for diagnosis. Multicentric studies are needed to a better knowledge of this tumour.

PS-01-069
Adenoid cystic carcinoma of the breast with an unusual clinical behavior
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Objective: Adenoid cystic carcinomas (ACC) of the breast are uncommon tumours with a paradoxically good prognosis. The optimal treatment of ACC has not yet been determined. A case report of an ACC of the breast is reported that recurred in the axilla, 2 years after simple mastectomy and a negative lymph node biopsy.
Method: A 73-year-old woman was referred to our hospital due to the mammographic finding of a 1,3 cm density of her left breast. The woman underwent a total mastectomy and sentinel lymph node biopsy. Two years later, the woman diagnosed with an enlarged lymph node of her left axilla. The woman underwent axillary lymph node dissection and chemotherapy.
Results: Histologic examination of the tumour density of the left breast was diagnostic of an adenoid cystic carcinoma of the breast. Sentinel lymph nodes were free of tumour deposits. FNA examination of the axillary recurrence was compatible with secondary nodal adenoid cystic carcinoma.
Conclusion: Lymph node and distal metastases of ACC in the breast are rare. We report for the first time a case of metachronous axillary recurrence after a negative sentinel lymph node biopsy. Our case shows that it is necessary for these patients to be closely followed-up and periodically examined following treatment.

PS-01-070
Expression of ANRIL "Polycomb Complexes" CDKN2A/B/ARF genes in breast tumours: Identification of a two-gene (EZH2/CBX7) signature with independent prognostic value
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Objective: We analyzed in invasive breast carcinomas (IBCs) expression of the long noncoding RNA (lncRNA) ANRIL that has recently been reported to have a direct role in recruiting polycomb repressive complexes PRC2 and PRC1 to regulate expression of the p15/CDKN2B-p16/CDKN2A-p14/ARF gene cluster.
Method: Expression analysis of ANRIL, EZH2, SUZ12, EED, JARID2, CBX7, BMI1, p16, p15, and p14/ARF genes was evaluated in a large cohort of invasive breast carcinomas (IBC, n ¼ 456) by qRT-PCR and immunohistochemistry (IHC) was performed on CBX7, EZH2, p14, p15, p16, H3K27me3, and H3K27ac.
Results: We observed overexpression of ANRIL (19.7 %) and EZH2 (77.0 %) and an underexpression of CBX7 (39.7 %). Correlations were identified between these genes, their expression patterns, and classical clinical and pathologic parameters, molecular subtypes, and patient outcomes.Multivariate analysis revealed that combined EZH2/CBX7 status is an independent prognostic factor (P ¼ 0.001). In addition, several miRNAs negatively associated with CBX7 underexpression and EZH2 overexpression. These data demonstrate a complex pattern of interactions between lncRNA ANRIL, several miRNAs, PRC2/PRC1 subunits, and p15/CDKN2B-p16/CDKN2Ap14/ ARF locus.
Conclusion: ANRIL is overexpression in 19.7 % of IBCs, presents a surprisingly strong positive correlation with p14 and combined EZH2/CBX7 status is an independent prognostic factor.

PS-01-071

Changes in expression of membrane-associated proteins connected to epithelial-mesenchymal transition during breast cancer progression

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Objective: It is characteristic for tumours to have impaired expression and exposition of E-cadherin and β-catenin due to epithelial-mesenchimal transition (EMT). We aimed at finding correlation between clinical features, progression risks and relapse of breast cancer and markers associated with EMT.
Method: We analyzed 45 cases of primary invasive carcinoma of no special type (IC NST) and 15 cases of distant metastases. Paraffin-embedded specimens were incubated with antibodies to main EMT markers (E-cadherin, β-catenin, α-SMA, vimentin)
Results: In areas of intercellular contacts tumour cells demonstrated weak diffuse positivity to E-cadherin. Further decrease in expression of E-cadherin was observed during tumour progression. Decrease in membrane expression and emergence of nuclear expression of β-catenin was observed in grade 2 and grade 3 carcinomas. Increased expression of actin and vimentin was present in 36,5 % of specimens (most from patients with stage IV of tumour progression). Least number of changes of expression or markers' disposition was observed in distant metastases.
Conclusion: Complete or partial loss of E-cadherin expression and reorganization of β-catenin are characteristic for late stages of IC NST. Actin and vimentin overexpression is associated with propagation and poor differentiation of tumours. Applied panel of markers may be used to analyze tumour progression.

PS-01-072

Cadherin and beta-catenenin expression in metastatic and nonmetastatic breast cancer

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Objective: The epithelial-mesenchymal transition entails disruption of E-cadherin and β-catenenin expression and distribution in the cancer cells.
Method: Immunohistochemical analysis of expression specifity, distribution and interaction of E-cadherin and β-catenin proteins in primary tumours of mammary glands was conducted. In our test group there were 32 (n = 32) matching cases (primary mammary gland tumours) and their metastases in lymphatic nodes (n = 4) and liver (n = 8).
Results: Expression of E-cadherin and β -catenin in mammary gland cancer cells was defined by immunohistochemical method. We discovered that reduction and complete absence of E-cadherin expression occurs more frequently in patients with mammary gland cancer who have developed metastases in liver (70 %) than in patients without metastases (30 %) (p = 0,014). The increase of cytoplasmic immunoreactivity and nuclear translocation of β-catenin was found in more than 80 % cases of mammary gland cancer, following the development of metastases.
Conclusion: These changes in E-cadherine and β-catenin expression in tumour cells could be considered as factors of unfavorable prognosis for mammary gland cancer. Expression of β-catenin indicates activation of signaling pathway, which is triggered by aberrant expression of epithelial cadherins. This leads to increase in mobility and invasive abilities of tumour cells.

PS-01-073

The clinicopathological features of invasive micropapillary carcinoma of the breast, a single center experience

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Objective: To summarize the clinicopathological findings of invasive micropapillary carcinoma of the breast
Method: The surgical excision specimens of 855 cases diagnosed between 2010 and 2016, were reviewed, retrospectively.
Results: We detected 48 cases with micropapillary component in at least 10 % of tumour (48/855; 6 %). Two out of 48 cases were male (2/48; 4 %). The ages ranged between 33–87 (median = 57,5). Tumour sizes ranged 0,6 to 9 cm (mean = 4,5 cm). T stages were as follows; T1:17; T2:24; T3:7. The involvement of sentinel and/or axillary lymph node was determined in 38 of 47 cases (80 %). N stages were; N0:9, N1:17, N2:10, N3:12. Histologic grade was 1 in 1 case, 2 in 28 and 3 in 19 cases. Nuclear grade was 2 in 19 cases and 3 in 28. Lymphovascular invasion was noted in 38 of 48(79 %). The molecular subclassification was ER(+)/HER2(-): 34(70,8 %), ER(+)/HER2(+): 5(10,4 %), ER(-)/HER2(+): 5(10,4 %), ER(-)/HER2(-): 4(8,3 %). Ki-67 index was 5 to 90 (mean = 28 %). P53 positivity was noted in 11 of 34 cases (32 %).
Conclusion: Our results were consistent with the literature in terms of the incidence of micropapillary carcinoma, the sex and age distributions, the presence of frequent lymphovascular invasion, frequent involvement of axillary lymph nodes at diagnosis and molecular subtype.

PS-01-074

Under-diagnosis and over-diagnosis in breast core needle biopsy: An estimation using inter-institutional whole slide imaging-based tele-consultation network

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Objective: Both false-positive and false-negative histological diagnoses can trigger serious consequences in breast cancer treatment. The aim of this study is to estimate the frequencies of under-diagnosis and over-diagnosis in core needle biopsy of the breast in major hospitals in Japan.
Method: A total of 615 consecutive core needle biopsies of breast performed in Nagoya Medical Center (n = 211) and Shikoku Cancer Center (n = 404) were used; all hematoxylin and eosin stained specimens were converted to whole slide imaging (WSI). All cases were classified into B1 to B5 categories on WSI independently by Drs. Nishimura and Ichihara who are specialized into breast pathology. When the categories determined on WSI by two specialists are identical, it was adopted as a central category. During 8 months' period between August 2015 and March 2016, a set of 615 breast core needle biopsies were diagnosed by 8 board certified pathologists of NHO using a teleconsultation network originally developed for tele-radiology.
Results: The under-diagnosis for invasive carcinoma, no special type (NST) and invasive carcinoma, special types (ST) were 3 and 2 %, respectively. The underdiagnosis for high, intermediate and low grade DCIS was 3 , 10 and 23 %, respectively. The overdiagnosis for radial scar/CSL and papilloma was 24 and 21 %, respectively. Although the overdiagnosis for phyllodes tumour/cellular fibroadenoma was 22 %, that for fibroadenoma was 0 %.
Conclusion: Underdiagnosis was less than 3 % in invasive carcinoma and high grade DCIS. However it was 10 and 23 % of intermediate and low grade DCIS, respectively. In addition, overdiagnosis occurred in about 20 % of benign or premalignant lesions concurrent with radial scar/CSL, papilloma and phyllodes tumour/cellular fibroadenoma.

PS-01-075

Does the BMI influence the overall survival in patients with primary invasive breast cancer?

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Objective: Obesity has been previously associated with increased risk of breast cancer, especially in postmenopausal patients but also inferior survival, including breast cancer-specific survival. The aim of the study is to evaluate the influence of the patients BMI on the overall survival in primary invasive breast cancer (IBC).
Method: We retrospectively reviewed the IBC identified in our database (2012–2015), diagnosed on a core biopsy, in which sentinel lymph node biopsy (SNB) and/or axillary lymph node dissection (ALND) was performed in association with surgical and oncologic treatment according to the tumour board suggestions. For comparison, all patients were divided into normal weight (NW) group (BMI < 25 kg/m2), overweight (OW) group (BMI 25-29.9 kg/m2) and obesity (OB) group (BMI ≥30 kg/m2), based on the WHO criteria.
Results: 100 patients were identified with follow-up (5 to 44 months), of which 30 patients were included in the NW (mean age 54.2), 37 in OW (mean age 59.2) and 33 in OB group. (mean age 62.57). 93 patients are alive (28 NW, 37 OW and 28 OB) and free of disease and 7 (5 OB and 2 NW) patients are deceased. There is significant difference in overall survival between these 3 groups and OB patients present a higher risk of death then NW and OW patients ($p = 0.0454$).
Conclusion: In our study, the overall survival of the patients is significantly influenced by the BMI of the patients.

PS-01-076
New gene signature for breast cancer molecular subtypes identification
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Objective: A number of gene signatures such as Oncotype DX (21 genes), MammaPrint (70 genes), PAM50 (58 genes), BluePrint (80 genes), EndoPredict (12 genes) are used to analyze gene expression and estimate the prognosis of disease recurrence, as reflected in the recommendations of St. Gallen (2017). We assume that to determine the molecular phenotype of breast cancer is sufficiently needed 10–12 genes and, as an example, we suggest one of the possible models.
Method: 151 tissue samples were studied (81 of breast cancer and 70 of normal-like breast tissue), of which 61 were native tissue samples and 90 FFPE tissue sections. Human mRNA species MKI67, MYBL2,CCNB1, CCND1, BIRC5, AURKA, TERT, CDKN2A, BCL2, BAG1, NDRG1, PTEN, MMP11, CTSL2, GRB7, ERBB2, SCGB2A2, MYC, ESR1, PGR, CD68, GUSB and B2M expression levels were measured using real-time qPCR with reverse transcription (DNA Technology JSC, Russia).
Results: In 81 % of cases the result of molecular subtype corresponded to IHC result (64/79). The most challenging was classification of the luminal subtypes. Sensitivity and specificity were 72–100 % and 90–99 %, respectively, depending on the molecular subtype of the tumour. The highest sensitivity and specificity were registrated in ERBB2-enriched and basal-like breast cancer phenotypes (100 and 99.2 % respectively). In 19.1 % of normal breast tissue samples molecular subtype was classified as tumour. A more precise classification of molecular phenotypes is possible by increasing the sampling and further optimization of investigated markers spectrum.
Conclusion: The proposed genetic signature of 15 genes from mRNA showed high sensitivity and specificity in determination of molecular breast cancer subtypes and validation can be recommended for clinical application.

PS-01-078
Pulmonary adenocarcinoma metastatic to the breast with divergent histological type
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Objective: Metastases to the breast from extra-mammary malignancies are very rare and generally show pathologic features of primary tumours. It is extremely uncommon when the metastatic tumour exhibit a different histological pattern from the primary neoplasm.
Method: We present the case of a 73 year-old woman who presented with a palpable tumour of her left breast with clinical suspicion of a second primary tumour, 6 months after she was diagnosed with a pulmonary adenocarcinoma of lepidic and micropapillary subtype, for which she was receiving chemotherapy.
Results: The patient underwent a core needle biopsy of the breast tumour, and histological examination revealed a pleomorphic high-grade carcinoma. Immunohistochemically, the neoplastic cells expressed cytokeratin 7, TTF-1 and napsin, and did not express ER/PR receptors and cerbB2. From her staging imaging control, she had no other evidence of metastasis and 4 months later she died due to pulmonary failure.
Conclusion: In conclusion, we report an extremely rare case of a pulmonary adenocarcinoma of lepidic and micropapillary subtype metastatic to the breast as a pleomorphic carcinoma. Distinguishing primary breast cancer from metastatic disease is critical in the management of patients with a known malignancy. Histopathologic features and clinical history in conjunction with the immunohistochemistry are mandatory in differential diagnosis.

PS-01-079
Immunohistochemical determination of breast cancer molecular subtypes in the clinical center of Montenegro
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Objective: To analyze gender and age distribution, as well as the distribution of molecular subtypes of breast cancer cases diagnosed at the Clinical Center of Montenegro.
Method: We analyzed all patients (256) diagnosed with invasive breast cancer in the period from January 2016 to March 2017. In patients who were planned for preoperative systemic therapy (74) the status of estogen receptor (ER), progesterone receptor (PgR), HER2 and Ki67 was determined on the samples obtained by core biopsy (CB). For patients in whom surgical treatment was initially planned (182), the determination of ER, PgR, HER2 and Ki67 was done on surgical samples (SS).
Results: All patients were female. The gratest number of patients were between 50 and 69 years old. The most common subtypes in the analyzed group were Luminal A (43.2 %) and Luminal B HER2- (29.7 %). Luminal B and triple negative breast cancer (TNBC) were more frequent in patients younger than 50 ($\chi2 = 11.751$; $p = 0.019$). No statistically significant difference in distribution of determined molecular subtypes was found between CB and SS ($\chi2 = 1.296$; $p = 0.8620$).
Conclusion: Two thirds of beast cancer cases are hormone positive, HER2-. Luminal B and TNBC subtypes are more frequently diagnosed in younger patients.

PS-01-080
Clinicopathological features of nipple adenoma in 5 cases
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Objective: Nipple adenoma (NA) is a rare, benign proliferative condition of lactiferous ducts of the nipple in middle-aged women with a history of serous or bloody nipple discharge. However, these lesions could mimic

malignancies both clinically and histopathologically. This study reports the clinical and histopathological features of 5 cases with NA.
Method: Five cases diagnosed as NA between 2010 and 2016 were reviewed retrospectively.
Results: All patients were women with ages ranged between 31 and 73 (median: 39, mean: 45). While 2 patients presented with palpable nodules, 3 patients had a history of ulcerative lesion and nipple discharge. Two cases were suspicious for Paget's disease, clinically. Microscopic examination revelead predominant growth patterns as in the form of papillomatosis in 2 cases, mixed in 2 cases and florid epitheliosis in 1 case. Sclerosing papillomatosis and pure type of adenosis patterns were not noted. Myoepithelial cells were displayed consistently with several markers (P63, smooth muscle actin, calponin) in all cases. An accompanying low grade Ductal Carsinoma in situ was determined focally in one of 5 cases.
Conclusion: To recognize the clinical presentation and the growth patterns of NA could help us to differentiate this lesion from the exact malignant proliferations.

PS-01-081
Metastin (KISS-1) expression in ductal carcinoma of the breast
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Objective: One of the most unfavorable forms of breast cancer is metastatic cancer. It occurs in 20–25 % of cases and is characterized by an aggressive clinical course and low survival rates, which attributes to aggressive biological phenotype. Metastin (KISS-1) is a gene, which suppresses metastatic activity of the tumour. We aimed at investigating the activity of metastin in ductal carcinoma of the breast.
Method: We have assessed the post-operative specimens of 30 women (age 28–63 years, the mean age was 49) with confirmed diagnosis of ductal carcinoma. Some of patients had regional and distant metastases. Metastin (Abcam) was used as primary antibody. Streptavidin biotin-peroxidase complex was used on paraffin sections of 3 mkm wide with additional staining of nuclei by hematoxylin.
Results: Intensity of the reaction was evaluated by semiquantitative method: (−) negative reaction, (+)—weak focal reaction, (++) average reaction, (+++)—intensive reaction with diffuse staining of cytoplasm. Intensive reaction was registered in 85 % of specimens of control group. In 9 specimens from patients who had confirmed metastases was registered weak focal reaction, remaining 21 specimens demonstrated intensive (1 case, 4,4 %), average (18 cases, 82,6 %) and weak (2 cases, 13,0 %) reactions.
Conclusion: Decrease in metastin expression in ductal carcinoma of the breast is associated with less favorable prognosis. Metastin can be used as an independent prognostic factor for survival and tumour metastatic potential in cases of breast cancer.

PS-01-083
Lymphovascular invasion in breast cancer after neoadjuvant chemotherapy. Review of 284 cases
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Objective: Lymphovascular invasion (LVI) is a poor prognostic factor in early breast cancer (BC). Recent studies have suggested it's also an independent predictive factor in survival after neoadjuvant chemotherapy (NACT). We studied the relationship of LVI with other pathological features, especially with early recurrence, in patients after NACT.
Method: BC cases from 2010 to 2016 were reviewed. Estrogen receptor, Progesterone receptor, HER2 and Ki67 were recorded. Pathological response (RCB score) and LVI were also reported.
Results: A total of 284 BC cases were reviewed, with a median follow up of 37,5 months. 5 were Luminal A, 133 Luminal B-Her2 negative, 70 HER2 positive and 76 Triple Negative tumours. 80 patients reached a pathological complete response, mainly in HER2 positive (54 %). Only 24 patients presented a relapse, and none of them died of disease. LVI was observed in 21 cases, with no correlation with disease free survival (DFS, $p = 0.116$) neither tumour intrinsic subtype ($p = 0.064$).
Conclusion: LVI didn't show any statistical correlation with early recurrence, probably due to the short follow up and low number of events observed. Further studies with a higher number of patients are needed to confirm the role of LVI in early recurrence and DFS in patients with BC after NACT.

PS-01-085
Spindle cell adenolipoma of the breast: Hitherto undescribed variant of mammary hamartoma
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Objective: Cutaneous spindle cell lipoma rarely shows ecrine and apocrine components. So far 9 such well-documented cases were reported in the literature and is called cutaneous spindle cell adenolipoma (Kazakov DV et al. 2011, Wilk M et al. 2013 etc). To our knowledge, spindle cell adenolipoma of the breast has not been reported.
Method: Here we present spindle cell adenolipoma in 63-year-old woman with histological and immunohistochemical work-up.
Results: The patient presented with a mass in the upper outer quadrant of the right breast. Ultrasound showed a well demarcated lobulated mass measuring 13.5 × 7.3 mm with a mixture of high and low echoic areas. There was no blood flow signal. Fine aspiration cytology was reported as negative. Excisional biopsy revealed a lesion composed of myxoid spindle cells, mature adipocytes and mammary glandular tissue.
Conclusion: Our case is a mammary analogue of cutaneous spindle cell adenolipoma. It can be viewed as a variant of breast hamartomas because it appears non-homogenous mass with circumscribed fatty mass.

PS-01-087
Breast cancer in patients aged 90 years and older: Pathological characteristics and molecular subtypes in a series of 40 cases
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Objective: There are few reports of breast cancer in women aged ≥90 years. The aim of this study was to investigate the pathological characteristics and molecular subtypes of breast cancer in this subgroup of patients.
Method: We reviewed the pathological files of invasive breast cancer in women aged 90 years and older between 2000 and 2016.
Results: Forty invasive breast cancer in women aged ≥90 years were identified. Mean age was 92 years (range 90–97). All cases were treated with mastectomy. Mean tumour size was 4.6 cm (range 0.4–15). Histologically, 77.5 % of cases were invasive ductal carcinomas. Fourteen cases were of histological grade 3. Lymph node metastases were present in 15 % of cases. Estrogen receptor (ER) and progesterone receptor (PgR) were positive in 67 and 55 % of cases, respectively. Overexpression/amplification of HER2 was observed in 10 % of cases. Mean Ki67 index was 16.8 % (range 3–75 %). Approximation of molecular classification yielded following results: luminal A, 33.3 %; luminal B/HER2-, 38.9 %; luminal B/HER2+, 5.5 %; ER-/PgR-/HER2+, 2.8 %; and basal-like, 19.4 %.

Conclusion: In conclusion, our results indicate that breast cancer in patients ≥90 years old exhibits larger size, high grade and prevalence of invasive ductal carcinoma. Molecular classification reveals a predominance of luminal B tumours in these patients.

Sunday, 3 September 2017, 09:30–10:30, Hall 3
PS-02 Endocrine Pathology

PS-02-002
Immunohistochemical study of 500 cases of neuroendocrine tumours
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Objective: Our study is an approach of grade and stage of neuroendocrine tumours diagnosed between Jan 2006 and Dec 2016 at Al-Assad university hospital/Damascus University, and to apply newly WHO approved classifications of these tumours depending on site of origin.
Method: We studied H&E stained sections, and multiple immunostains (Synaptophysin, Chromogranin, CD56, and CKs) to confirm the type, mitotic activity was evaluated by light microscopy and Ki-67.
Results: The patients age range between 18 and 72 year old, male to female ratio 312:188. The first three sites of higher incidences of primary neoplasias were Lung with 211 case, then GI tract and Pancreas with 131 case, the adrenal glands with 70 case, the remaining cases were presented in the thyroid, hepatic metastases, brain metastases and abdominal masses. Synaptophysin showed positive reaction on 90 % of studied cases,Chromogranin on 78 % and CD56 on about 54 % . Ki-67 evaluation felt into three groups : less than 3 % for well differentiated low grade tumours (204 case), 3 to 20 % for intermediate grades (121 case), and more than 20 % of high grade (175 case),high-grade nearly always presents with high-stage.
Conclusion: Neuroendocrine tumours are unique tumours that need to be confirmed by available methods and techniques, and given a meticulous evaluation of grade and stage, because of what that may affect the prognosis of the patient case and method of treatment.

PS-02-003
Papillary thyroid microcarcinoma: Retrospective study
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Objective: Papillary thyroid microcarcinoma (PTMC) is defined after its size till 10 mm or less. PTMC diagnosis increased in pathology routine concerning almost 50 % of all papillary carcinomas. In near future, accurate diagnosis correlated with histopathological variants and prognosis parameters.
Method: A series of 369 PTMC was reviewed as a retrospective 10 years study in Centro Hospitalar e Universitário de Coimbra, collected from thyroid carcinomas surgical specimen and reclassified according to the 8th AJCC of the 2017. Histophatological type, patient gender/age, bilaterality and mutifocality were the searched parameters.
Results: Female gender prevalence (87,3 %) was consist as already known and 56 years (between 21 and 80 years old) was the medium age. Multifocal tumours were found in 25,7 % (19,6 % bifocal, 5,1 % trifocal and 1 % with more than three tumours) of cases. Histopathologically we found non encapsulated follicular PTMC, non encapsulated classical type, encapsulated classical and encapsulated follicular variants in 46.6 %, 27.4 %, 11.9 and 11.1 % respectively. All cases of the PTMC were now reclassified as pT1a.
Conclusion: These results are in accordance with international casuistic. The increasing incidence of PTMC is actually due to the improvement of the clinical diagnostic acuity, together with the increase of surgical procedures and pathology concern.

PS-02-004
Differential diagnosis between benign and malignant thyroid nodules using Second Harmonic Generation Microscopy
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Objective: The purpose of this study was to compare the ultrastructural capsular changes appearing in follicular adenoma, papillary and follicular thyroid carcinoma for differentiating between benign and malignant thyroid nodules.
Method: Second Harmonic Generation(SHG) Microscopy was used to image collagen distribution in the capsules of several types of nodules. The tissue fragments were formalin-fixed, paraffin-embedded but without H&E staining, with 4–7 microns thick sections. Collagen organization was evaluated using different parameters such as the collagen organization coefficient based on the Fast Fourier Transform(FFT) of 2D-images and the Gray-Level Co-Occurrence Matrix(GLCM) angular second moment(ASM) used as a measure of textural uniformity and entropy which is a parameter of disorder in a micrograph.
Results: SHG microscopy images were acquired to assess the collagen organization of tumoural capsular thyroid nodules previously diagnosed as benign or malignant by conventional H&E staining. Different degree of collagen fibers organization was observed and quantified using FFT and GLCM. A higher degree of structural variation was observed for the thyroid capsule compared to nodular capsules resulting in lower value of ASM and higher entropy.
Conclusion: These above described microscopy method help us distingues between benign or malignant thyroid nodules, based on the capsular colagen parameters, especially in patients treated with antithyroid drugs.

PS-02-006
Immunohistochemical expression of CD1a in different tumours of pituitary gland
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Objective: Recently it has described that expression of CD1a could be useful to distinguish adenomas from non-neoplastic pituitary parenchyma, with positive staining in normal parenchyma and negative staining in adenomas. In our study we analyzed the immunohistochemical expression of CD1a in tumoural and normal pituitary samples with the aim of verifying the utility of this staining in different lesions of hypophysis.
Method: Immunohistochemical staining was performed using the automated staining device Ventana BenchMark Ultra (Roche Diagnostics, Mannheim, Germany) and the antibody was the rabbit antibody against CD1a (clone EP3622, Roche Diagnostics).
Results: A total of 24 samples (13 adenomas, 8 normal hypophysis, 2 atypical macroadenoma and 1 craniopharyngioma) were analyzed. Three adenomas were completely negative for CD1a staining and 10 cases showed scattered positive cells. All cases of normal tissue showed positivity for CD1a. Moreover we found that the 2 atypical macroadenomas showed intense CD1a immunoreactivity and the craniopharyngioma sample showed isolated positive cells.
Conclusion: In our study we found that CD1a is not a very useful marker for distinguishing adenomas from normal tissue hypophysis, because we found scattered positive cells the majority of adenomas and the craniopharyngioma and diffuse positivity in two cases of atypical macroadenomas.

PS-02-007
The usefulness of parathyroid hormone measurement in fine needle aspiration biopsy washout fluids of parathyroid neoplasm

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Objective: Primary hyperparathyroidism is caused commonly by a solitary adenoma and less commonly by hyperplasia of the parathyroid glands. The management of primary hyperparathyroidism is surgical. Minimally invasive parathyroidectomy (MIP) requires the clear localisation of a parathyroid lesion. Ultrasound (US)-guided fine needle aspiration biopsy (FNAB) can successfully localize abnormal parathyroid tissue. This technique can be limited by the coexisting goiter and previous surgical procedures in the neck. The measurement of parathyroid hormone (PTH) levels in needle washout fluids has been reported to increase the diagnostic accuracy of FNAB in preoperative localizing of pathological parathyroid glands and their discriminating from thyroid tissue and neck lymph nodes.
Method: FNAB/PTH samples from 27 patients with primary hyperparathyroidism and one patient with suspicious of parathyroid carcinoma metastasis were evaluated and compared with subsequent surgery.
Results: Twenty six patients yielded elevated PTH level > 3000 pg/ml. Twenty three of these patients underwent MIP, and 3 patients are awaiting a surgical procedure. Histopathologic examination of excised abnormal parathyroid tissue confirmed parathyroid adenoma in 20 and hyperplasia in 3 patients.
Conclusion: The combined approach of cytology and measurement of PTH levels in needle washout provides high diagnostic accuracy in the interpretation of US-guided FNAB for preoperative localisation of parathyroid lesions.

PS-02-008
GATA-3 immunoreactivity expands the transcription factor profile of pituitary neuroendocrine tumours
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Objective: The classification of pituitary neuroendocrine tumours (pitNETs) uses immunohistochemistry for transcription factors, adenohypophyseal hormones and other biomarkers. The transcription factor GATA-2 is required for the development of gonadotrophs and thyrotrophs but to our knowledge has not been used in the diagnosis of pitNETs. Because of the genomic paralogy of GATA-2 and GATA-3, we postulated that antibodies to GATA-3 may detect GATA-2 in pitNETs. For this reason, we investigated the expression profile of GATA-3 in a series of pitNETs.
Method: A series of 81 pitNETs (26 gonadotroph, 24 somatotroph, 17 corticotroph, 12 lactotroph, and 2 poorly differentiated Pit-1 lineage tumours that expressed beta-TSH) was investigated with a monoclonal GATA-3 antibody using an automated stainer. Nuclear positivity for GATA-3 was scored as follows: 0 (0–5 %), 1 (6–25 %), 2 (26–50 %), 3 (51–75 %), and 4 (>75 %).
Results: With the exception of a few entrapped non-tumourous adenohypophyseal cells, all corticotroph, somatotroph, and lactotroph tumours lacked GATA-3 expression. All gonadotroph tumours were positive (score 4). Two poorly differentiated Pit-1 lineage tumours that expressed beta-TSH were also positive for GATA-3 (score 3).
Conclusion: This cohort showed that GATA-3 identifies positivity in gonadotroph tumours and in poorly differentiated Pit-1 lineage tumours that express beta-TSH. This finding is important in the differential diagnosis of sellar tumours since GATA-3 expression has been reported in paragangliomas/pheochromocytomas, parathyroid proliferations and carcinomas that may metastasize to the sella. Further studies are required to clarify the distinction of GATA-2 and GATA-3 in this application.

PS-02-009
Evaluation of the expression of transcription factors of neuro D1, Pitx1 and Pit1 in human pituitary adenomas
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Objective: to evaluate the expression of Neuro D1, Pitx1 and Pit1 in corticotropinomas, gonadotropinomas and prolactinomas.
Method: We studied 5 prolactinomas, 5 gonadotropinomas, 8 corticotropinomas and 5 normal adenohypophysis of 8 men and 15 women (the mean age was 45 ± 13 years). The immunohistochemistry was performed using antibodies against Ki-67, Neuro D1, Pitx1, Pit1 and the six hormones of the anterior pituitary.
Results: The expression of Neuro D1 was observed in 90 % of gonadotropic cells, in 85 % of prolactin cells, in 94 % of corticotropic cells and in 39 % cells of the normal adenohypophysis, on the average. The expression of Pitx1 was found in 19 % of prolactin cells, in 4 % of corticotropic cells, in 13 % of the normal adenohypophysis, on the average, and was not observed in gonadotropic cells. The Pit1 expression was observed in 0,45 % of prolactin cells, in 16,5 % cells of the normal adenohypophysis, on the average, and was not detected in gonadotropinomas and corticotropinomas. There was not any significant correlation between the expression level of transcription factors and Ki-67.
Conclusion: The transcription factors Neuro D1, Pit1 and Pitx1 remain important for the normal adenohypophysis in adult humans. Neuro D1 may play a crucial role in the pathogenesis of various pituitary adenomas.

PS-02-010
CD-immunophenotype of infracentimetric parathyroid cysts associated to lymphocytic parathyroiditis: Relevance for pathogenesis
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Objective: We aimed to report immunohistochemicaL features of infracentimetric parathyroid cysts identified in parathyroid adenomas associated to lymphocytic parathyroiditis, resected for hyperparathyroidemia and hypercalcemia.
Method: The parathyroid specimens were studied for chromogranin, CD10, CD31, CD56, CD68 and CD324/E-cadherin immunohistochemistries.
Results: Chromogranin and CD324 were expressed heterogeneously in the cyst or vesicle parathyroid cell lining. In one of the cases, CD10 and CD56 were expressed by the luminal membrane of parathyroid cells. CD31, as well as CD68, were expressed in monocytes/macrophages located dispersely between parathyroid cells (interparathyroid sinusoids) or in parathyroid vesicles. Several monocytes/macrophages expressed also CD10 and/or CD56.
Conclusion: In conclusion, heterogeneous CD324 expression in parathyroid cells may only indirectly be related to vesicle and cyst formation while CD56 and CD10 expressions seem incidental. The relevance of the sinusoid/intravesicular monocyte/macrophage-type cells phenotype (CD31-, CD68-, CD10- or CD56-positive) for vesicle/cyst formation and/or associated lymphocytic parathyroiditis remains to be further investigated.

PS-02-011
Encapsulated variant of papillary thyroid carcinoma with spindle cell metaplasia: A case report with review of the literature
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Objective: We want describe a case of this very rare entity focusing on the differential diagnosis
Method: Having a large nodule on the right lobe, a 77 years old patient was referred to surgery. Macroscopically a well demarcated tan-yellow

8.5 cm nodule has been observed. Necrosis or invasive pattern have not been seen. Formalin fixed, paraffin embedded tissue samples of the tumour have been examined in the H&E routine stain. To support the final diagnosis immunohistochemistry was also performed.
Results: Microscopically the encapsulated tumour was characterized by follicles with thyreocytes that showed larger nuclei, sometimes irregularly spaced, clear chromatin and "grooves". Focally, spindle cells were noted which did not show mitoses. Interestingly these cells are positive for-TTF-1 and thyreoglobulin. The neoplasm showed focal capsular and vascular-invasion and was positive for HBME-1 and galectin-3.
Conclusion: To our best knowledge only one case of encapsulated variant of papillary thyroid carcinoma with spindle cell metaplasia was previously published. Herein we report another case summarizing the morphological and immunohistochemical characteristics that help to differentiate it from more aggressive spindle cell proliferations such anaplastic thyroid carcinoma.

PS-02-012
CD56 - a novel marker in differential diagnosis of hyalinising trabecular tumour
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Objective: Hyalinizing trabecular tumour (HTT) is an uncommon thyroid neoplasm and a diagnostic challenge—both on cytology and histopathology. Numerous nuclear inclusions, pale chromatin and occasional nuclear grooves are suggestive of papillary carcinoma. Atypical (membranous) reaction in Ki-67 immunohistochemical test is conclusive. The aim of the study was to establish the diagnostic value of markers commonly used for differentiation between papillary carcinoma and hyperplastic nodules, in evaluation of HTT.
Method: 13 cases of HTT, in which immunohistochemistry revealed membranous expression of Ki-67 in tumour cells, were diagnosed in years 2008–2016 in the Department of Tumour Pathology of the Institute of Oncology and qualified for the present study. For each specimen a test with Ki-67 was repeated and staining with CK19, CD56, Galectin, HBME, Chromogranin and Synaptophysin was performed.
Results: Tumour cells showed strong membranous expression of Ki-67 and CD56 in. respectively, 12/13 and 13/13 cases. Cytoplasmic reaction with Chromogranin concerned 13/13 cases. Extratumoural tissue revealed membranous expression of CD56, but only HTT cells were positive for Chromogranin and Ki-67.
Conclusion: Immunohistochemical tests with CD56 and Chromogranin may be conclusive in diagnosis of hyalinizng trabecular tumour if characteristic membranous expression of Ki67 is weak or completely absent.

PS-02-013
Clinicopathological patterns of adrenal gland tumours among Sudanese patients
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Objective: To describe the common clinicopathological pattern of adrenal gland tumours among Sudanese Patients.
Method: Retrospective study of 37 adrenal tumours diagnosed at laboratories in Khartoum State in the period from January 2007 to March 2015. After consent archived H&E slides were retrieved and reviewed. The data was collected into a detailed questionnaire and analyzed.
Results: The most common incidence was among the age group less than 10 years (29.7 %), followed by the age group 30–39 years (21.6 %). The mean age was 27.1 years and 70.3 % were females. Excisional biopsy was the common type of specimen (86.5 %) followed by tru-cut biopsy (13.5 %). The most common clinical presentations were high blood pressure and abdominal mass. Most tumours (51.4 %) are 5–10 cm. Most tumours are medullary (70.3 %) with 62.2 % benign, 35.1 % malignant and 2.7 % metastatic. Pheochromocytoma was the most common benign tumour (35.1 %), followed by adrenocortical adenoma (13.5 %), and ganglioneuroma (8.1 %). Adrenocortical carcinoma and ganglioneuroblastoma represented 10.8 % each among the malignant cases, while neuroblastoma and malignant pheochromocytoma contribute 8.1 and 5.5 % respectively.
Conclusion: Pheochromocytoma is the commonest benign tumour in the age group 30–39 years (38.5 %). Adrenocortical carcinoma was the commonest malignant tumour in the age group 20–29 years. Neuroblastoma and ganglioneuroma are the commonest malignant tumours in the <10 years age group.

PS-02-014
New insights in the clinical and translational relevance of miR483-5p in adrenocortical cancer
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Objective: Adrenocortical cancer (ACC) is a rare aggressive malignancy. Recent ACC integrated genomics analysis contributed to redefine the risk groups on molecular basis, including tumour microRNAs (miRs), detectable also in the bloodstream.
Method: We developed a quantitative real-time (RT) assay for the measurement of miR483 and miR483-5p absolute levels in plasma samples. miR483/miR483-5p levels were evaluated in plasma samples of 27 patients with ACC before surgery and at follow-up.
Results: Statistically significant differences in miR483-5p and miR483 levels were found between stage 1/2 and stage 3/4 ACCs in pre-surgery and post-surgery samples. ROC curve analysis of miR483–5p levels gave a prediction of the clinical stage (accuracy 0.917 ± 0.084), with the best cut-off value of 0.221 ng/ml, prognosticating overall and recurrence-free survival. In a multivariate Cox analysis (HR 16.2, 95%CV[1.39-188.6, $P < 0.026$]). miR483-5p was the only variable that significantly predicted recurrence, but not overall survival, In addition, miR483 and miR483-5p levels correlated with the number of circulating tumour cells (CTCs) detected in the same blood samples, independently of the timing of sampling.
Conclusion: In conclusion, we demonstrated that miR483-5p absolute plasma levels in ACC patients are powerful molecular markers that may help in the follow-up of patients after surgery and chemotherapy, and contribute to more accurately classify and predict tumour progression.

PS-02-015
Validation of a panel of genes identified by miRNA profiling as candidate prognostic biomarkers in lung carcinoids
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Objective: To validate the role of four genes, uncovered in a previous study as specific targets of miRNAs differentially expressed in lung carcinoids, as novel prognostic biomarkers
Method: In silico analysis was performed to predict a panel of candidate genes regulated by miR-409-3p and miR409-5p, which were shown by our group to be associated with aggressive disease, by using at least 5 online software programs and their biological properties or potential role in carcinogenesis. The genes identified (CREBp1, ACVR2B, LHX2 and KFL12) were analyzed using real-time PCR in a cohort of 89 lung carcinoids and correlated with clinical-pathological parameters and disease-free survival
Results: High levels of ACVR2B and LHX2 and low levels of KLF12 were significantly associated with atypical histotype, higher tumour grade

and higher mitotic index (all $p < 0.05$). ACVR2B increased in patients with higher proliferation index ki-67 ($p = 0.006$). Moreover, low levels of KLF12 and high levels of CREBp1 were associated with presence of necrosis ($p < 0.01$). Finally, low KLF12 expression was associated with shorter survival at univariate analysis ($p = 0.003$), together with male sex, atypical histotype and the presence of vascular invasion (all $p < 0.01$)
Conclusion: ACVR2B, LHX2 and KFL12 are novel potential biomarkers associated with aggressive disease in lung carcinoids

PS-02-016
MGMT promoter methylation and expression in a large series of lung neuroendocrine neoplasms
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Objective: To investigate the gene and protein expression of MGMT in lung neuroendocrine neoplasms, in association with clinical and pathological characteristics.
Method: A retrospective series of 146 surgically resected lung neuroendocrine neoplasms was analyzed for MGMT promoter methylation by means of pyrosequencing, MGMT gene expression by means of quantitative real time PCR and MGMT protein expression using immunohistochemistry.
Results: Using a cut-off of >5 % methylated sites, 51 % showed MGMT hypermethylation either in the whole series or in the group of carcinoids only. A significant inverse correlation was observed between gene promoter methylation and protein expression (Spearman $r = -0.29$, $p = 0.001$) but not with gene expression. The number of methylated sites progressively increased from carcinods to high grade carcinomas, whereas MGMT gene expression was significantly increased in large cell neuroendocrine carcinomas (all $p < 0.02$). In carcinoid group only, MGMT hypermethylation was associated with lower stage and negative nodal status ($p < 0.002$) whereas lower MGMT gene expression was associated with atypical histotype, high stage, and positive nodal status (all $p < 0.02$).
Conclusion: Decreased MGMT gene expression is associated with aggressive disease in lung neuroendocrine neoplasms, and the high proportion of lung carcinoid cases with MGMT promoter methylation supports the use of alkylating agents for their treatment.

PS-02-017
EGFR mutation in anaplastic thyroid carcinoma
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Objective: Anaplastic thyroid carcinoma (ATC) is a rare but extremely aggressive and lethal tumour which has no effective treatment. Epidermal growth factor receptor (EGFR) mutations are commonly used for targeted therapy in lung adenocarcinoma. EGFR mutations were investigated in ATC for therapy and a few data of this relation in the literature. The aim of this work was to investigate the presence of EGFR mutations in ATC.
Method: In a retrospective study, we studied 32 patients who were diagnosed with thyroidectomy or biopsy-proven ATC between 2002 and 2017. EGFR mutation status in exons 18,19, 20 and 21 was examined from the paraffin blocks of 32 patients by using a real-time PCR (Cobas® 4800).
Results: Of 32 patients, 15 were female and 17 were male. The mean age was 67 years (age range 49–83). Survival time ranged from 1 to 17 months with a mean of 4.4 months. We detected no EGFR exon 18,19, 20 and 21 mutations in 32 cases.
Conclusion: These data support the absence of EGFR mutations in ATC. This should be taken into account when considering targeted treatment of ATC.

PS-02-018
Histopatological features and molecular abnormalities in thyroid tumours developed after exposure to external radiation
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Objective: To compare morphological and molecular characteristics between thyroid tumours occurring after radiation exposure and sporadic tumours.
Method: 41 tumours (19 adenomas and 22 differentiated carcinomas (DTC)) of patients with a history of radiation therapy and 51 control tumours (24 adenomas and 27 DTC) were analyzed. Molecular analysis was performed using NGS.
Results: Median age at radiation exposure and at diagnosis was 10 and 31 years, respectively. Papillary thyroid carcinoma was diagnosed in 18/22 radiation-exposed and 27/27 sporadic cases. Tumour size, mitotic index, vascular invasion, extrathyroidal extension, lymph node metastases and multifocality were not different between groups. 43 genetic abnormalities were identified: 25 fusions and 18 point mutations (BRAF, HRAS & NRAS hotspot mutations). In radiation-exposed tumours, 1 fusion was found in adenomas, and 12 fusions and 2 point mutations in DTCs, including a previously unreported fusion KIAA1468/RET in 2 cases. In sporadic tumours, 1 fusion and 6 point mutations were found in adenomas, 11 fusions and 10 point mutations in DTCs. RET/PTC1 ($n = 6$) and RET/PTC3 ($n = 7$) were the most frequent fusion transcripts in DTCs.
Conclusion: Sporadic and radiation-exposed thyroid tumours present similar histopathologic features and genetic abnormalities, whereas point mutations might be more frequent in sporadic cases.

PS-02-019
Clinicopathological features of incidental papillary thyroid microcarcinoma
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Objective: Papillary thyroid microcarcinoma (PTMC) is characterized by an indolent clinical course and an excellent prognosis. However, some PTMCs behave aggressively. The aim of the study was to investigate clinicopathological characteristics possibly related with aggressive behavior in PTMC.
Method: A total of 1166 patients who underwent total thyroidectomy (2011–2016) were reviewed retrospectively. Of these, 144 patients with PTMC (M/F 28/116, mean age 50.5, range 19–75 years) were enrolled in the study. Clinicopathological features were evaluated by univariate analysis.
Results: The prevalence of PTMC was 12.3 %; the great majority of cases were incidental (132/144). The mean tumour size was 3.3 ± 2.3 mm (range 0.1–9.0 mm). Multifocal disease was observed in 42 patients (29.2 %), bilateratility in 21 (14.6 %), infiltrative tumour border in 81 (56.3 %), capsular invasion in 28 (19.4 %), <1 mm distance from resection margin in 47 (32.6 %), positive resection margin in 12 (8.3 %), extrathyroid extension (ETE) in 16 (11.1 %), follicular growth pattern in 86 (59.7 %), calcifications in 24 (16.7 %) and lymphocytic thyroiditis in 48 (33.4 %). Capsular invasion and infiltrative tumour border were correlated with ETE ($p < 0.001$ and $p = 0.005$, respectively).
Conclusion: Histopathological evaluation of incidental PTMC may reveal high risk factors (extrathyroid extension, positive resection margin, subcapsular location) for tumour recurrence and/or lymph node metastasis.

PS-02-020

The expression of tumour-associated macrophages and multinocleated giant cells in papillary thyroid carcinoma

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Objective: Inflammation that occurred in the tumour microenvironment was characterized by abundant macrophage infiltration, playing role in innate immunity. Multinucleate giant cells (MGCs) occur in a variety of inflammatory, hyperplastic, and neoplastic thyroid disorders. They also have been recognized as a feature of papillary thyroid carcinoma (PTC). The aim of this study was to evaluate cases of PTC for the presence of macrophages, and estimate CD68+ TAMs density in tumour stroma, margin and the surrounding tissue. We assessed also MGCs. Macrophages and MGCs densities were correlated with clinicopathologic parameters to assess the possible prognostic significance.
Method: We investigated 81 patients (12 (14.8 %) men and 69 (85.2 %) women) from 22 to 81 years immunohistochemically and immunofluorescence with antibodies against CD68 and IL-17.
Results: A statistically significant correlation was established between PTC patients in III and IV stage, containing many MGCs, and PTC in I and II stage, with many MGCs. 80 % of patients in III and IV stage showed many MGCs in comparison with patients in I and II stage, where many MGCs were found only in 21,1 % ($\chi 2 = 6.189$, $p = 0.013$).
Conclusion: Our study demonstrates that the increased density of MGCs is associated with advanced stage of PTC, and therefore with tumour progression and that cases of PTC should be carefully screened for their presence.

PS-02-021

Involvement of leptin receptor expression in neoangiogenesis and parathyroid hormone levels in parathyroid carcinoma

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Objective: The aim of this study is to evaluate the expression of leptin receptors (LEPR) in parathyroid carcinoma (PC) and the correlation of their expression with neoangiogenesis and level of parathormone (PTH) in plasma.
Method: On the biopsy specimens of 10 patients surgically treated for PC in the Center for Endocrine Surgery, Clinical Center of Serbia, were applied the routine HE and immunohistochemical ABC method with anti-LEPR and anti-CD105 antibodies. After the quantitative analysis of LEPR expression, the microvascular density (MVD) per mm2 was calculated stereometrically. All patients had elevated levels of PTH (mean 1824 pg /ml). For the statistical analysis of obtained results the software package SPSS (version 20.0) was used.
Results: Prominent or moderate LEPR expression was found in 40 % of the PC. The high index of neoangiogenesis (mvd IDX) is in the significant correlation ($p < 0.001$) with pronounced expression of LEPR. The increase in LEPR expression is accompanied by increase in PTH levels. Expression of LEPR is with a highly significant correlation coefficients associated with mvdIDX and PTH levels. ($r = 0.58$ and $r = 0.61$).
Conclusion: Significant correlation of LEPR expression with the index of neoangiogenesis and PTH levels in PC may have significant therapeutic and prognostic implications.

PS-02-022

Ecto-5′-nucleotidase (CD73) is overexpressed in papillary thyroid cancer

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Objective: The ectoenzyme CD73 (EC 3.1.3.5, ecto-5′-nucleotidase, 5′ NT) is considered a promotes of tumour progression and notably, is frequently overexpressed in various cancer types but its role in papillary thyroid cancer (PTC) remains understudied. The aim of this study was to evaluate the CD73 expression in PTC compared with their adjacent non-tumour thyroid tissue.
Method: Thirty-one cases of primary PTC were analyzed by immunohistochemistry for CD73 expression using monoclonal antibody. The main diagnostic criteria for PTC are the characteristic nuclear features like grooves, intranuclear cytoplasmic inclusions, ground glass appearance and the papillary architecture may or may not be present. Staining intensity was graded as 0 (negative), 1 (weak), 2 (modarate), and 3 (strong).
Results: All tumour samples were positive for CD73 staining with weakly positive in 1 (3.2 %), moderate positive in 11 (35.5 %) and strongly positive in 19 (61.3 %). Adjacent non-tumour tissue present staining for CD73 negative in 15 (48.4 %) and weakly positive staining in 16 (51.6 %) cases.
Conclusion: These preliminary results showed an elevated CD73 expression in PTC when compared with non-tumour thyroid tissue and its clinical significance in PTC requires further analysis.

PS-02-023

Expression of CD9 and CD82 in papillary thyroid microcarcinoma and its prognostic significance

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Objective: Papillary thyroid microcarcinoma is one of the well-known malignant neoplasms with good prognosis. The known prognostic factors are patient age, multifocality extrathyroidal extension. CD9 and CD82, members of the tetraspanin family, are expressed in numerous cancer cells and play many roles associated with cellular process.
Method: We collected the cases of 553 PTMC patients who had undergone thyroidectomy from January to December 2010 at the Severance Hospital (Seoul, South Korea). We investigated the immunohistochemical expression of CD9 and CD82 in papillary thyroid microcarcinoma and analysed the clinicopathologic and prognostic significance.
Results: The group with lymph node metastasis showed higher immunostaining intensity for CD9 than the group without metastasis ($p = 0.002$). In multivariate analysis, high CD9 intensity (OR = 1.58 in 3+, $p = 0.0025$) were correlated with lymph node metastasis.
Conclusion: We suggest CD9 as a predictive prognostic factor for lymph node metastasis in PTMC. Further studies with other cancers will be needed to determine the exact function of CD9.

PS-02-024

Peculiarities of expression of PDX-1 in neuroendocrine and non-neuroendocrine tumours of different localisation

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Objective: The homeodomain transcription factor PDX-1 plays a key role in endocrine and exocrine differentiation processes of the pancreas, it is essential for differentiation of endocrine cells in the gastric antrum, but in normal corpus mucosa it is mainly absent
Method: We investigated expression PDX-1 in 173 neuroendocrine (NET) end 48 non-neuroendocrine tumours of different localisation by immunohistochemical method.
Results: Among PDX-1-positive NETs were 95,4 % (84/88) tumours of the pancreas, 48 % (12/25) stomach, 100 % (12/12) duodenum, 75 % (3/4) rectum; all the rest NETs were negative—small and large intestine (0/17), lung (0/17), Merkel carcinomas (0/10). PDX-1-positive were

71,4 % (10/14) adenocarcinomas of the pancreas, 50 % stomach (4/8), 33,3 % (2/6) large intestine. All adenocarcinomas of the lungs (0/4) and solid pseudopapillary tumours of the pancreas (0/16) were PDX-1-negative

Conclusion: The obtained data indicates that the clear organo- and tissue-specific expression of PDX-1 is available for NETs of pancreas, duodenum and rectum. PDX-1 expression is also observed in half of the NETs of stomach, which probably originate from the antrum. The peculiarities of PDX-1 expression allow to determine more accurately the origin of metastases without a known primary localisation. PDX-1 is overexpressed in many types of cancer, including pancreatic, stomach, intestinal, but not of the lungs cancers.

PS-02-025

Preoperative diagnosis of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

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Objective: The purpose of this study was to determine whether noninvasive follicular thyroid neoplasm with papillary-like nuclear feature (NIFTP), invasive encapsulated follicular variant papillary carcinoma (I-EFVPTC), and infiltrative FVPTC (IFVPTC) could be distinguished by preoperative diagnostic tests.

Method: 258 tumours comprised of 89 NIFTPs, 77 I-EFVPTCs, and 92 IFVPTCs were included in our study. Preoperative evaluations were ultrasonography (US, TIRADS Category), fine needle aspiration cytology (FNA, Bethesda System), core needle biopsy (CNB, Category of Korean endocrine pathology thyroid CNB study group), and molecular test.

Results: NIFPT and I-EFVPTC relatively revealed AUS/FLUS or follicular neoplasm in FNA and CNB, low or intermediate suspicious for malignancy in US, and RAS mutation. IFVPTC had relatively high rates of suspicious for, or definite malignancy in FNA and CNB, high suspicious for malignancy in US, and BRAF mutation and RET/PTC rearrangement. NIFTP and I-EFVPTC were difficult to distinguish by preoperative studies. We found that the significant predictors of IFVPTC were cyto-histologic study (FNA + CNB) and US, and that molecular test had no predictive power.

Conclusion: NIFTP and I-EFVPTC were difficult to distinguish from each other before surgery, but they could be distinguished from IFVPTC by FNA + CNB and US, which could help clinicians plan for surgical treatment.

PS-02-026

Higher prevalence of incidental thyroid papillary microcarcinoma in males. A systematic autopsy study

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Objective: Clinical thyroid cancer (TC) is increasing worldwide. Its incidence in women is about three-fold greater than in men. It is not clear if this increase is due to a greater sensitivity in diagnosis or is a true increase. We studied the prevalence of TC in autopsies.

Method: We systematically investigated the thyroid gland of 155 patients who had no previously known thyroid clinical pathology. After fixation all glands were cut in 4–5 mm sections and totally paraffin embedded. All paraffin blocks were stained with hematoxylin-eosin, thyroglobulin, calcitonin and/or PTH.

Results: There were 106 (68.4 %) males studied and 49(31.6 %) females with an average age of 62.4 years (range: 1–97). Micropapillary carcinoma (mPC) was found in 45(29.03 %) patients, 32(20.6 %) males and 13(8.4 %) females. Bilateral mPC was encountered in 10(6.4 %) cases (7 males, 3 females). One (0.6 %) medullary microcarcinoma was also found.

Conclusion: The high prevalence of mPC in this autopsy series suggests that the increase of clinical TC is due to a greater sensitivity of diagnostic techniques. This high prevalence of mPC in males (20.6 % vs 8.4 %) contrasts with the greater prevalence of clinical TC in women, suggesting hormonal factors involved in the promotion of clinical TC. Grant PI15/01501-FEDER from ISCIII, Spain.

PS-02-028

Histopathological correlates of paediatric non-medullary thyroid cancers in an endemic goiter region

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Objective: The rarity, clinical and molecular characteristics of thyroid cancers in the paediatric age group (≤18 years) have brought an interest into this subject. We investigated histopathological correlates of a series of paediatric non-medullary thyroid cancer in an endemic goiter region from Turkey.

Method: A retrospective review of records of three tertiary centers between 2009 and 2016 identified 38 thyroidectomy specimens with pediatric non-medullary thyroid cancers. Demographic features, gross and microscopic findings were recorded.

Results: The average age was 15.61 years with a male-to-female ratio of 6:32. The mean tumour size was 2.98 cm. While poorly differentiated thyroid carcinoma was seen in one patient, 37 had papillary thyroid carcinoma (PTC) including 7 microcarcinomas (PMC). Among those 32 displayed classical (25 classical, 4 diffuse-sclerosing, 2 Warthin-like, and 1 hobnail cell variants), 3 displayed follicular (3 infiltrative follicular variant), and 3 had solid (3 solid variant) growth patterns. Two PTC had focal dedifferentiation. Multifocality was noted in 14 patients; 12 of which were PMC. The overall rate of PMC was 39.47 %. Vascular and lymphatic invasion was noted in 13 and 24 tumours. Eighteen and seven patients had metastatic nodal disease and extra-thyroidal extension, respectively.

Conclusion: The predominance of classical architecture suggested that BRAF-like phenotype (as defined by the TCGA cohort) was the most common correlate of paediatric thyroid carcinomas in an endemic goiter region. From an epidemiological perspective, the absence of non-invasive follicular variant PTC (currently known as NIFTP) and a relatively high frequency of PMC (~40 %) were also important highlights of this series.

PS-02-029

Immunohistochemical study of the lymphocytic microenvironment in papillary thyroid carcinoma, associated or not with thyroiditis

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Objective: Thyroid cancer is usually surrounded by a significant number of immune reactive cells. Tumour associated lymphocytes as well as background lymphocytic thyroiditis is frequently mentioned in pathology reports of patients operated for thyroid cancer. Evidently, the fact that cancer can survive in this adverse microenvironment speaks for immune regulation. The aim of this study was to investigate the prognostic value of the lymphocytic infiltration that accompanies human papillary thyroid carcinoma (PTC) and compared it to that present in human autoimmune thyroid disease or Hashimoto thyroiditis (HT).

Method: CD4+, CD8+, and FOXP3+ lymphocytes were assessed by immunohistochemistry in tumour tissue from 36 patients with PTC.

Results: Positive immunostaining was detected in lymphocytic cells of the tumour and of the non-tumour adjacent lymphoid tissue. In general, the expression of FOXP3 presented increased distribution in a larger percentage of biopsies when carcinoma lesions were associated with HT. Of the clinicopathological parameters analyzed the expression of FOXP3 correlated only with tumour stage (p = 0,03).
Conclusion: The expression of FOXP3 was significantly upregulated in biopsies with PTC associated HT compared with carcinoma without association, suggesting that may play an important role in the pathology of PTC injuries, exerting influence on the aggressiveness of the tumour.

PS-02-030
Analysis of biochemical composition of adrenal gland tumours by infrared microspectroscopy
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Objective: The objective of the study was to verify the idea of using Fourier Transform Infrared (FTIR) microspectroscopy for medical analysis of biomolecular markers and try to differentiate non-neoplastic and neoplastic cortical and medullary lesions in adrenal gland.
Method: Tissue samples taken intraoperatively from patients with adrenal adenoma, adrenal hyperplasia and pheochromocytoma were used in the study. The specimens were cut into sections of 10 μm thick in a cryomicrotome and mounted on silver coated sample supports (Low-e MirrIR, Kevley Technologies). Biochemical composition was investigated using infrared (FTIR) microspectroscopy.
Results: We found the differences in absorption spectra for two spectral ranges: between 2997 and 2800 cm-1, which corresponds to the lipids bands and between 1770 and 1485 cm-1, which are assigned mainly to the amides bands. Higher level of the ratio of alpha/beta secondary protein structure in adenoma samples comparing to pheochromocytoma and hyperplasia was detected as well as decreased glycogen/phosphate ratio for adenoma and hyperplasia samples comparing with pheochromocytoma.
Conclusion: FTIR microspectroscopy is a suitable method for the study of biomolecular composition of adrenal gland lesions. Adrenal tumours deriving from cortical and medullary cells differ within the range of lipids as well as proteins absorption bands.

PS-02-032
Utility of CD56 as diagnostic marker in nodular thyroid lesions
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Objective: to determine utility of CD56 immunostain in distinguishing between papillary thyroid carcinoma (PTC) and benign lesions.
Method: 75 formalin-fixed-paraffin-embedded tissues samples with 22 PTC (18 follicular variant and 4 conventional PTC), 3 follicular carcinomas, 2 medullary carcinomas, 49 normal parenchyma, 17 follicular adenomas, 10 Hurthle cell adenomas, 35 nodular hyperplasia, 15 lymphocytic thyroiditis, 1benign cyst, 8Graves' disease, 1lymph node metastasis from PTC, 1benign thyroid inclusion in lymph node and 1parathyroid gland were analyzed and immunostained against CD56 antibody. Membranous staining was considered positive were more than 10 % of examined cells showed immunoreactivity.
Results: Loss of CD56 staining was observed in 15 PTC (68 %) (13 follicular variant and 2 conventional PTC), 1Hurthle cell adenoma, 1benign cyst and 1normal parenchyma. CD56 was expressed in all follicular and medullary carcinomas, 48normal parenchyma, 17follicular and 9Hurthle cell adenomas, 35nodular hyperplasia, 15 lymphocytic thyroiditis, 8Graves' disease, 1lymph node metastasis, 1benign inclusion and the parathyroid gland. Statically significant difference detected in CD56 expression between PTC and benign lesions ($p < 0.0001$) and PTC and other thyroid carcinomas ($p = 0.0098$). Sensitivity was 68.2 %, specificity 97.2 %, positive predictive value 79 % and negative predictive value 95.2 %
Conclusion: CD56 is helpful in distinguishing PTC and its follicular variant from benign nodular lesions.

PS-02-034
Encapsulated follicular variant papillary thyroid carcinoma with atypical cells
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Objective: Atypical cells can be seen in various thyroid pathologies such as toxic goiter, radiation change, dyshormonogenetic goiter, follicular adenoma and anaplastic thyroid carcinoma. However, atypical cells are rare in papillary thyroid carcinomas(PTC), and only an article had been published that presents four cases. It was presented five cases of encapsulated follicular variant PTC with atypical cells.
Method: Five cases of PTC with atypical cells were detected in examined thyroidectomy specimens between 2005 and 2017. The clinical and pathologic findings and survive were investigated.
Results: One of the patient was male, others were female. The mean age was 30 years (range 14–50). All the patients were treated with I131 ablation once and no recurrence was detected in the 5-year follow-up. Histologically, PTC was seen as encapsulated nodules between 2.5 and 6.7 cm in diameter in all cases. The nodules was composed of follicles showing nuclear features of PTC. In some follicles, there were atypical cells with large, hyperchromatic and pleomorphic nuclei.
Conclusion: Despite the presence of atypical cells, these tumours do not differ in survival from other encapsulated follicular variant PTC. However, PTC with atypical cells should be kept in mind that it can be confused with anaplastic thyroid carcinoma, especially in cytologic diagnosis.

PS-02-035
A rare type of thyroid tumour: Primary epithelioid angiosarcoma
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Objective: The primary angiosarcoma of the thyroid is a malignant tumour with endothelial differentiation. It is often observed in Alpine countries of Central Europe, generally in patients with prolonged nodular goiter associated with iodine deficiency. In this report, morphologic and proteomic findings of primary thyroid angiosarcoma are discussed with its differential diagnosis.
Method: A 47-year-old male patient had neck and ear pain for 1 year. Ultrasonography revealed a poorly circumscribed hypoechoic mass at the thyroid right lobe-isthmus. FNA biopsy was positive for malignancy and total thyroidectomy and right functional neck dissection were performed.
Results: Gross findings showed that a 3.5 × 2.7 × 1 cm solid mass with irregular margins and hemorrhagic areas completely filled the right lobe and extended to the isthmus. Histopathologically, the mass was consisted of atypical mesenchymal cells with eosinophilic cytoplasms with partly fusiform, partly epithelioid features and chromatin-rich nuclei. Scattered multinucleated tumour cells were also observed. Immunohistochemically, tumoural cells were positive for CD31, Fli-1 and vimentin; focally positive for D2-40, pancytokeratin and CD34 and negative for TTF1, thyroglobulin, Pax-8, cytokeratin20, HBM45 and CEA. Systemic scanning of the patient revealed no other lesions and with the morphological and

immunohistochemical findings the patient was diagnosed as primary thyroid angiosarcoma.
Conclusion: Primary thyroid angiosarcoma causes difficulties in the differential diagnosis, because they imitate the pseudoangiomatous patterns and the reactive atypical and benign vascular proliferations occurring with primary and secondary thyroid malignancies. Since primary thyroid angiosarcoma has different clinical, histological and immunohistochemical features, its differentiation from undifferentiated carcinoma is particularly important.

PS-02-036
Composite pheochromocytoma-ganglioneuroma of the adrenal gland: Case report
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Objective: Composite pheochromocytoma (CP) is a rare tumour that combines features of pheochromocytoma with those of ganglioneuroma (>70 % of cases), ganglioneuroblastoma, neuroblastoma or peripheral nerve sheath tumour.
Method: We present a case of composite pheochromocytoma-ganglioneuroma of the right adrenal gland of a 37-year-old male patient. Grossly an encapsulated tumour arising from the adrenal gland was observed, measuring 4.5 × 4 × 2 cm and weighing 20 gr. The cut surface was tan brown partially pale.
Results: Microscopically the tumour was composed predominantly of areas with features of pheochromocytoma, focally exhibiting pronounced nuclear pleomorpism. A second component intermixed with the pheochromocytoma was identified, consisting of ganglion-like cells, in a fibrillary schwannian stroma arranged in transverse bundles. Immunohistochemicaly the pheochromocytoma cells were positive for Chromogranin-A and Synaptophysin. Staining for neurofilament proteins highlighted the ganglion cells and axon-like processes. S-100 was expressed in the sustentacular and schwann cells.
Conclusion: The histogenesis of composite tumours has been attributed to the common embryologic origin of the chromaffin and neuronal cells. Differentiation of pheochromocytoma cells into neuronal cells has been also suggested. CPs are often associated with familial neoplasm syndromes (neurofibromatosis type 1 or multiple endocrine neoplasia type 2A). Composite tumours containing ganglioneuroma without immature neural elements have the same prognosis as pheochromocytoma.

PS-02-037
Ultrastructural features of cellar interactions in pancreatic insulinomas
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Objective: Pancreatic insulinomas
Method: Tumours of 38 patients who had been in the surgical treatment from 2010 to 2015 was studied. Male to female ratio was 10:28. The average age was 48.2 years. All the tumours were clinically benign. The electron and histological study of the removed tumours was conducted.
Results: In 39,5 % the tumour was localized in the head, in 24 % - in the tail, in 36 % - in the body. Tumour's size ranged from 0.8 to 5.5 cm. G1 was present in 84 %. G2 was present in six cases. Ultrastructurely two main β-cell phenotypes in different stages of functional activity were detected: "the light cells" were dominated by the processes of synthesis of granules; "the dark cells", in which the processes of hormone secretion outside the cell membrane were actively running. The two cell types were connected by the desmosomal junctions. In the area of contact of adjacent cell's cytomembrane the portions of the cytoplasmic fusion with the formation of cytoplasmic bridges were determined. This resulted in the formation of syncytium-like structures. These changes were more common between "the light cells".
Conclusion: Through the cytoplasmic bridges the metabolic processes of nutrients and secretory material occure. Perhaps, it is a condition for the release of granules synchronization processes in the bloodstream. Syncytium-like structure due to the large size cannot penetrate through the fenestrated capillary, eliminating the possibility of the formation of the secondary tumours. Moreover, their production makes it impossible to complete the next cell division and progression of the tumour stops.

PS-02-038
Metastasis in a cervical lymph node of two metachronous primary tumours
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Objective: We present a case of two metachronous metastatic tumours in the same lymph node,a clear renal cell carcinoma and a papillary thyroid carcinoma
Method: A 72 years old male patient underwent nefrectomy for a clear renal cell carcinoma with contemporary presence of adrenal glands metastasis and multiple vascular tumour emboli. One and a half year later the same patient was treated surgically for an FNA diagnosed papillary thyroid carcinoma.The thyroid gland and cervical region IV lymph nodes were send to our laboratory.
Results: A papillary thyroid carcinoma of follicular variant was found histologically with involvement of 4 cervical regional lymph nodes. One of them was occupied by synchronous metastasis from a clear renal cell carcinoma formerly diagnosed to the patient.
Conclusion: Multiple primary malignant tumours are clinicopathological conditions of great interest both for their biology and for their clinical significance. An accurate histologic evaluation and the use of Immunohistochemistry in correlation with clinical history of the patient will help avoid pitfalls.

PS-02-039
Composite pheochromocytoma of the adrenal gland
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Objective: We present a rare case of composite pheochromocytoma of the adrenal gland.
Method: A 62 year old woman presented to our hospital with hypertension. 24 h urine collection showed increased metanephrines while Computed Tomography revealed an adrenal mass. We received an adrenal gland measuring 12 × 12 × 2.5 cm and weighting 55 gr. The cut section was fleshy in consistency and yellowish-orange to tan, with four discreet lesions, the largest one being partially cystic. The two smallest lesions had nodular appearance in admixture with grossly normal adrenal gland.
Results: Microscopically the findings were compatible with pheochromocytoma and ganglioneuroma coexisting with nodular hyperplasia of the adrenal gland. Immunohistochemistry was performed with Chromogranin A, Synaptophysin, Inhibin-A, NSE, S-100, GFAP, Melan-A, CD56. Ki 67(MIB1) proliferation index was estimated 1,5 %. Scoring was 3 according to Adrenal Gland Scoring Scale PASS (Thompson 2002).
Conclusion: Composite pheochromocytomas are rare. The biologic behavior of these tumours may be as difficult to predict as that of more traditional pheochromocytomas. Therefore it is suggested that composite pheochromocytomas may be regarded as a histologic variant of classic pheochromocytoma.

PS-02-040

Hyalinising trabecular tumour: A rare tumour of the thyroid gland

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Objective: Discuss the histological criteria of hyalinizing trabecular tumour (HTT) and emphasize diagnostic difficulties.
Method: A 48 years old female patient, with a medical history of breast cancer, presented with a lump in the left side of the neck.
Results: Ultrasonography revealed an heterogeneous left isthmolobar nodule. Isthmectomy was performed. Gross investigation showed an encapsulated mass of 3 × 2 × 1 cm. The cut surface was homogeneously pale and rigid. Microscopically, the nodule was encapsulated. No capsular or vascular invasions were observed. The tumour was characterized by trabecular structures separated by fibrous stroma with many calcifications. The intra-trabecular hyalin was prominent with PAS positivity and Congo Red negativity. Alveolar structures were also present, partitioned by sinus vascular network. The tumour cells were oval with an acidophilic or clear cytoplasm. The nuclei were round with frequent pseudoinclusions. Immunohistochemical study showed positivity for thyroglobulin and negativity for calcitonin, synaptophysin, chromogranin A, galectin 3 and hormone receptors. MIB-1 staining showed a distinctive membranous pattern. The diagnosis of HTT was made after eliminating metastasis of breast cancer, papillary and medullary thyroid carcinomas.
Conclusion: HTT represents a rare and controversial thyroid tumour easily confused with papillary or medullary thyroid carcinoma. Awareness of this entity will allow a better classification and management.

PS-02-041

Adrenal myelolipoma: A case report

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Objective: Adrenal myelolipoma (AM) is a rare benign tumour that mostly solitary, asymptomatic, unilateral and non-secreting. Histologically, it is composed of hematopoietic precursor cells and mature adipose tissue. The increased use of screening systems, such as ultrasonography, computed tomography and magnetic resonance imaging (MRI), the incidental detection is increasing in frequency.
Method: We report a case of adrenal giant mass that detected incidentally in 44-year-old female with no symptoms. There was no finding in physical examination. Abdominal MRI scan revealed a well-demarcated, round shaped lesion which was 10 × 8 cm sized and located in left adrenal region with heterogenous attenuation suggesting the possibility of myelolipoma. The patient was subjected to left adrenalectomy.
Results: In gross examination, the specimen was round-shaped, encapsulated mass with smooth external surface measuring 10,1 × 8 × 5,7 cm. Cut surface revealed a solid tumour with a heterogenous appearance of dark brown and yellowish areas. In histopathologic examination, the tumour composed of bland-looking hematopoietic precursor cells and mature adipose tissue.
Conclusion: Although AM is considered to be a rare tumour, widespread use of imaging modalities and sensitivity of this equipments resulted in relatively increase of this entity.Therefore pathologists should consider this tumour in differential diagnosis of adrenal tumours.

PS-02-043

Mary I of England and her tumour: A brief historical and clinicopathological review

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Objective: To discuss the disease that was behind the death of Queen Mary I of England and Ireland (1516–1558).
Method: Historical records, mainly dated from the 17th century, and books were reviewed to identify signs and symptoms associated with Mary's disease. After that a clinicopathological correlation was done trying to establish her underlying cause of death. Moreover, a brief histopathological review about possible diseases was done.
Results: Mary Tudor was the eldest child of King Henry VIII of England. Since her childhood, Mary suffered from emotional disorders. Queen Mary believed herself to be pregnant for twice, but no child ever born. During Mary's I life her main symptoms were: amenorrhoea, depression, headaches, palpitation, indigestion, blurry vision, swelling of the abdomen and milk secretion. So possible diseases are: an ovarian tumour, an hydatiform mole or a prolactinoma. Combining all these symptons we favour a prolactinoma as the tumour behind her death.
Conclusion: Mary Tudor was ill since May 1558. In suffering, possibly from an advanced prolactinoma, she died on 17 November 1558. Probably her direct cause of death was a pituitary apoplexy, a clinical entity first coined in 1950 by Brougham, 45 years later of the first case reported by Bleibtreu.

Sunday, 3 September 2017, 09:30–10:30, Hall 3
PS-03 Gynaecological Pathology

PS-03-001

A review on new pattern based endocervical adenocarcinoma classification: Our experience

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Objective: Endocervical adenocarcinomas are currently staged according to the depth of invasion(DOI). Lately a new patern based classification system was proposed as assesing DOI can be quite challenging and difficult from case to case. We reevaluated our cases to this new classification to investigate the efficacy.
Method: Case selection was made using our institute's database. Patients who have undergone radical surgery with lymph node resection were chosen. Only the usual type endocervical adenocarcinoma was included. 6 cases were involved in this study. Cases were reevaluated according to the 3 tiered system and correlated with DOI, lymph node metastasis and lymphovascular invasion.
Results: Of the 6 cases 3 were classified as Pattern A, 1 was Pattern B and 2 of the cases were Pattern C. None of the patients with Patterns A or B had lymph node metastasis and lymphovascular invasion. On the contrary Pattern C patiens had lymphovascular invasion and 1 of them had lymph node metastasis. There was no association between DOI and patterns.
Conclusion: Currently endocervical adenocarcinoma management is based on DOI and it is the single most important decisive factor in lymph node resection. Since it is a highly discomforting procedure for patients this new patern based staging may be a better alternative on this call. Additional large case series and worldwide use of this system must be encouraged.

PS-03-002

Diffuse large B cell lymphoma with plasmablastic differentiation of the cervix uteri: A case report and review of the literature

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Objective: Differentiation between diffuse large B cell lymphomas (DLBCL) with plasmablastic differentiation and true plasmablastic

lymphomas is difficult. It is also concluded that this types of lymphomas have predilection to HIV-positive individuals and may be strongly associated with HHV8 and EBV. Plasmablastic differentiation is associated with poorer prognosis.
Method: We report a case of a 34 year-old HIV-negative woman with 6 cm cervical mass and systemic lymphadenopathy of thoracic and abdominal cavity. A biopsy from cervical mass was taken.
Results: Histologically there were tumour fragments of solid growth character with rich lymphoid infiltration. Tumour cells were medium sized with characteristics of plasmacells and immunoblasts (pankeratin and HMB-45 negative). Tumour cells were positive for CD45, CD38, BCL-6, Mum1 and CD10 with restricted expression of Lambda Light Chain. CD20 expression was negative, MIB-1 expression was high (90 %). The diagnosis was made in favor of DLBCL with plasmablastic differentiation.
Conclusion: This case is worth attention due to rare localisation of tumour and complicated immunohistochemistry. Differential diagnosis should include plasmocytoma (CD10 negative) and other types of diffuse large B-cell lymphomas.

PS-03-003
Unusual morphological changes of uterine leiomyomas treated with ulipristal acetate: Delineation of new characteristic histological features
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Objective: Ulipristal acetate (UPA) is an oral selective progesterone-receptor modulator (SPRM). Progesterone receptor modulators (PRM) are hormonally active drugs effective in the management of uterine leiomyomas (ULMs). The histological endometrial changes associated with PRM treatment have been described as PAEC (PRM Associated Endometrial Changes), but the morphological features of ULMs treated with PRMs are currently not well-defined. The aim of the study was to describe and evaluate the PRM-associated changes in ULMs.
Method: Here, the histopathological features of ten ULMs treated with UPA are reported.
Results: In all patients ULMs were multiple, lesions greater than 5 cm showed grossly marked cyst appearance and were more softened and paler than the usual leiomyoma. The morphological changes included vascular alterations (thick-walled blood vessels, lymphangioma-like appearance of the vessels, intravascular thrombi, contraction of the muscular wall of the vessels), and degenerative alterations of the intratumoural stroma such as cystic formation, marked stromal oedema, mixoid change and/or hyalinization. Rarely, apoplectic changes (multiple stellate to ovoid zones with a hypercellular periphery and central hemorrhage, mitotic activity, pyknosis and necrosis) were observed.
Conclusion: In order to appropriately classify these benign tumours, pathologists should be aware of PRM-associated morphological changes in ULMs that may represent a response to the treatment. Furthermore, these unusual features and cystic changes could explain the initial unmarked reduction in size of the lesions that clinicians may interpretate as treatment failure, leading to an unnecessary histerectomy.

PS-03-004
Tumour immune surveillance in lymphoepithelioma-like carcinoma of the uterine cervix: Utility of RNA-Scope® in-situ hybridisation, quantitative PCR and immunohistochemistry
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Objective: Compared to conventional squamous cell carcinoma, lymphoepithelioma-like carcinoma of the uterine cervix has a better prognosis, a lobular syncytial pattern and a heavy inflammatory infiltrate. We aimed to identify the involved inflammatory populations and their topography.
Method: The inflammatory population was analyzed in 3 cases by an extensive panel of immunohistochemistry (IHC), by RNAscope® in situ hybridization (ISH) and by a wide-range quantitative PCR (qPCR).
Results: On standard IHC, CD3-positive lymphocytes predominated over few clusters of CD20-positive lymphocytes. Most CD3-positive lymphocytes were CD8-positive, often infiltrating the tumour, and coexpressing GranzymeA and GranzymeB. CD4-positive lymphocytes were found around tumour lobules and coexpressed FoxP3. CD56-positive lymphocytes were found around tumour lobules. CD68-positive macrophages were found abundantly within and around tumour lobules. On RNAscope® ISH, the secretion of Interferon-γ was more important within and around tumour lobules, compared to Interleukin-10. On qPCR, CD8 was most expressed compared to CD4 and CD19. The cytotoxic (GranzymeA and GranzymeB) and regulatory (FoxP3, Interleukin-10, TGF-β1, TGF-β2, TGF-β3) markers predominated compared to T-helper1 (Interleukin-2, Interferon-γ, Interferon-α), T-helper2 (GATA3, Interleukin-4, Interleukin-5, Interleukin-6, Interleukin-13) and T-helper17 (Interleukin-17A, Interleukin-22) markers.
Conclusion: High tumour-infiltrating cytotoxic and peritumoural regulatory T-cells can ensure a successful tumour immune surveillance, explaining the good prognosis of lymphoepithelioma-like carcinoma.

PS-03-005
Endometrioid carcinoma with unusual patterns and cell types: A diagnostic challenge
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Objective: Endometrioid carcinoma (EC) is the most common subtype of endometrial carcinoma (70–80 %) and accounts for 10–15 % of ovarian carcinomas. The majority of ECs share typical microscopic features, but unusual patterns and cell types have been described and represent a diagnostic challenge.
Method: We report 6 cases of EC, describe their morphological features and issues in the differential diagnosis.
Results: Case 1: 66-years-old. Endometrial EC with cords and hyalinized stroma. Main differential diagnosis (MDD): carcinosarcoma. Case 2: 51-years-old. Endometrial EC with small nonvillous papillae. MDD: serous carcinoma. Case 3: 76-years-old: Papillary endometrial EC. MDD: serous carcinoma. Case 4: 67-years-old. Endometrial EC with signet-ring cells. MDD: Gastrointestinal adenocarcinoma metastasis. Case 5: 60-years-old. Ovarian EC with architectural patterns similar to those of sex cord-stromal tumours. MDD: sex-cord stromal tumours. Case 6: 54-years-old. Ovarian EC with clear cells. MDD: clear cell carcinoma.
Conclusion: The accurate diagnosis of EC has therapeutic and prognostic implications. Awareness of EC wide morphologic spectrum and adequate sampling to find more typical areas, in the majority of cases, aids in the differential diagnosis. In some cases, immunohistochemistry can also be helpful.

PS-03-007
Ovarian steroid cell tumour in an adolescent with von Hippel-Lindau syndrome: A case report and review of the literature
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Objective: Von Hippel-Lindau (VHL) syndrome is an autosomal dominant genetic disorder caused by germline mutation of the VHL gene. It's associated with multiple neoplasias including haemangioblastoma, clear

cell renal carcinoma (CCRC), pheochromocytoma and neuroendocrine tumours. Ovarian tumours are extremely rare in this syndrome.
Method: We describe the case of an adolescent with VHL syndrome and ovarian steroid cell tumour.
Results: Sixteen-year-old girl had the diagnosis of bilateral pheochromocytomas and multiple pancreatic neuroendocrine tumours in VHL syndrome context. Follow-up abdominal-pelvic MRI revealed a 33 mm, well circumscribed nodule in the right ovary. The patient was submitted to laparoscopic right salpingo-oophorectomy. Microscopically the tumour consisted of polygonal cells with abundant microvacuolized clear cytoplasm arranged in a solid pattern. The neoplastic cells were immunohistochemically positive for inhibin and calretinin and negative for CD10, excluding the possibility of metastatic CCRC. A diagnosis of ovarian steroid cell tumour was made. Only three cases with this association have been reported. Unlike our case, they described adult women with VHL syndrome who presented with secondary amenorrhoea and hirsutism due to testosterone-secreting ovarian steroid cell tumours.
Conclusion: Although extremely rare, association between VHL syndrome and ovarian steroid cell tumour has been reported and this may suggest a link between the two entities.

PS-03-008
Three concurrent gynaecological malignancy with intraabdominal gastrointestinal stromal sarcoma
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Objective: Synchronous or metachronous multiple primary malignancies are infrequent. Multiple primary malignant neoplasm are defined as a diagnosis of two or more independent primary malignancies of different origins in an individual. To the best of our knowledge, this is the first case in the English literature of three concurrent gynecological malignancy with intraabdominal gastrointestinal stromal sarcoma.
Method: A 49-year- old perimenopausal woman, with previous medical history of intra-abdominal gastrointestinal stromal sarcoma operation 8 years ago and history of using imatinib for this purpose. She underwent operation for her second recurrens GIST. During the operation, surgeons noticed tubal mass next to recurrens GIST mass.
Results: Final pathology report of tubal mass was ESS and incidental ovarian mass as borderline endometiroid carcnoma. Complementary hysterectomy and left salpingoooferectomy were made. Which revealed at uterin as atypical endometrial hyperplasia and left ovary as serous borderline carcinoma.
Conclusion: These tumours in the patient that are different from each other and do not have known common etiology. Endometriosis and adenomyosis foci detected in the patient may play a role in the etiology of some tumours. However, genetic counseling should be performed in patients with such synchronous / metachronous tumours.

PS-03-009
Unusual bilateral ovarian metastases from ileal gastrointestinal stromal tumour (GIST)
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Objective: Ovarian metastases from GIST are very rare. Two cases of GIST metastatic to the ovary are reported highlighting the pathological and molecular features.
Method: We retrospectively reviewed data of 224 female GIST patients collected from 2001 to 2017; two cases of GIST with ovarian metastases are described.
Results: GIST primary site was the ileum in both cases and the ovarian localisations were multiple and of small dimension (0,5–2 cm of diameter), grossly yellowish, solid, with circumscribed borders. Microscopically, the tumours were composed by a proliferation of stromal spindle cells arranged in short fascicles, with pale, occasionally vacuolated eosinophilic cytoplasm and mild atypia. The differential diagnosis included ovarian stromal tumours, granulosa cell tumour with fibromatous stroma, localisation of leiomyoma or leiomyosarcoma. Considering the coexisting ileal GIST, immunohistochemical stains for DOG-1 and c-Kit were also performed resulting strongly and diffusely positive. The final diagnosis was GIST (spindle cell type) of small bowel with bilateral ovarian metastases. In both cases a KIT exon 11 c.1674_1695del mutation with a consequent Lys558_Gly565 deletion was found by direct Sanger sequencing.
Conclusion: Ovarian metastasis from GIST, even if rare, can be a challenging diagnosis both for pathologists and clinicians that should be aware for the significant therapeutic and prognostic implications.

PS-03-010
Yolk sac tumour concurrent with a mature teratoma in same ovary: A case report
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Objective: Yolk sac tumour (YST) is a rare malignant germ cell neoplasm that most commonly occurs in women in the second and third decades. These tumours are usually pure but may be part of a mixed gem cell tumour, usually with dysgerminoma. Mature teratoma is the most common type of ovarian germ cell neoplasm. The combination of YST with mature teratoma is very rare.
Method: We report a case of YST concurrent with mature teratoma in same ovary in a 25-year-old woman.
Results: A 25-year-old woman presented with an irregular menstrual cycle and a pelvic mass. CT scan revealed an ovarian tumour of 13,5 cm in diameter. At the periphery of the mass another cyst associated with fatty areas and calcifications , indicating teratoma.The serum level of alpha-fetoprotein was elevated(108050 ng/mL). Surgery was performed.Microscopically, the first tumour showed a typical papillary, reticular (microcystic), glandular pattern, hyaline globules and Schiller-Duval bodies. Immunohistochemistry of the tumour revealed expression of AFP , Glypican-3, SALL-4 while beta-HCG, cytokeratin 7 and cytokeratin 20 were negative. Second mass had a typical histomorphological features of mature teratoma.
Conclusion: We report to our knowledge, the third case of YST concurrent with mature teratoma in same ovary.

PS-03-011
Immunohistochemical prediction for concurrent endometrial carcinoma on biopsy samples with endometrial intraepithelial neoplasia
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Objective: Our aim was to investigate whether immunohistochemistry could predict the existence of concurrent endometrial carcinoma in patients with an initial diagnosis of endometrial intraepithelial neoplasia (EIN) on endometrial biopsy samples
Method: We retrospectively selected 55 biopsy samples diagnosed with EIN, from patients who subsequently underwent radical hysterectomy in our clinic. On the hysterectomy specimen, 29.09 % (n = 16) of the patients presented concurrent endometrial and 70.91 % (n = 39) were diagnosed with either EIN, non-atypical endometrial hyperplasia or other

benign lesions. Immunostaining for Ki-67, PTEN, p53, bcl-2 and MMR proteins was performed.
Results: Patients with concurrent endometrial carcinoma had well and moderately differentiated variants of endometrioid carcinoma. PTEN-loss was identified in 13 out of 16 EIN cases (81.25 %) with concurrent endometrial carcinoma and 20 out of 39 EIN cases (51.28 %) that proved benign. Ki-67 revealed increased cellular proliferation restricted to the areas of PTEN-loss. For patients with concurrent endometrial carcinoma, p53 overexpression was identified in 5 cases (31.25 %), while MLH1 and PMS2 inactivation was observed in 3 (18.75 %), respectively 2 cases (12.5 %).
Conclusion: Endometrial biopsies presenting EIN with increased nuclear atypia and PTEN-loss are more likely to be finally diagnosed with endometrial carcinoma. Prediction may be even more accurate when Ki-67 and p53 expressions are considered simultaneously.

PS-03-012
Cervical lymphocyte populations of HIV positive women: Are they related to HPV co-infection and cervical cancer?
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Objective: To characterize lymphocyte subsets in endocervical cytobrush (EC) samples of HIV+ women, comparing them according to the presence of HPV and cervical lesions.
Method: 18 HIV+ and 13 HIV- women EC samples were characterized using monoclonal antibodies (CD3,CD4,CD8,CD16/CD56,CD19,CD45) by a 4-color BD FACS Calibur, with a Paint-a-Gate. HIV+ Peripheral blood CD subsets, viral load, cervical cytologies and HR HPV typing were also studied. Statistical analysis: GraphPadPrism 6 software with significance considered for $p < 0.05$.
Results: In HIV+ women, different percentages of CD4 ($p = 0.0479$) and CD8 T-cells ($p = 0.0007$), and CD4/CD8 ratios ($p = 0.0081$) were found between PB and EC samples. Nevertheless, parameters varied similarly and were significantly correlated in both sample types (CD4: $p = 0.0004$,$r = 0.7610$; CD8: $p = <0.0001$,$r = 0.8710$; CD4/CD8 ratio: $p = 0.0020$,$r = 0.763$). Higher percentages of circulating CD8 T-cells ($p = 0.0460$) and a trend for lower CD4/CD8 ratios ($p = 0.0568$) were observed in HIV+ women with HSIL/LSIL, compared to HIV+ women negative for intraepithelial lesion or malignancy (NILM).
Conclusion: We identified CD4 and CD8 cervical lymphoid populations that are correlated with their circulating counterparts. Cervical CD4 T-cells and CD4/CD8 ratios were found to be decreased in HIV+ women. Higher percentages of circulating CD8 T-cells seem to be related with the presence of squamous intraepithelial lesions in HIV+ women, and eventually to HR-HPV.

PS-03-015
Improving reproducibility of diagnosis of differentiated Vulvar Intraepithelial Neoplasia (dVIN): Morphological features and immunohistochemistry (cytokeratin 13 and 17)
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Objective: To find the most specific and reproducible morphological features for the difficult histopathological diagnosis of dVIN. We also assessed the feasibility of combination of cytokeratin 13 (CK13) and cytokeratin 17 (CK17) immunohistochemistry as diagnostic markers for dVIN.
Method: Cases of dVIN ($n = 180$), lichen sclerosus (LS) ($n = 105$) and other chronic inflammatory conditions ($n = 126$) were reviewed from the archives of Erasmus MC (2010–2013). Individual histological features were enumerated from a predetermined check list, and statistical comparison between dVIN and inflammatory lesions was made. Inter-observer agreement between two pairs of experienced pathologists was assessed. Participants recorded the individual features they found most useful. CK13 and CK17 immunohistochemistry was performed (32 dVIN, 14 LS, 8 other inflammatory cases).
Results: We found good inter-observer agreement for the diagnosis of dVIN (Weighted Kappa = 0.71). Nuclear angulation, mitotic count >5/5 mm, and features of disturbed maturation were statistically significant as compared to reactive conditions, and were deemed the most useful. For dVIN, about 70 % cases showed CK13 loss coupled with CK17 expression. LS did not show this pairing.
Conclusion: Our study determines the histological features to separate dVIN from reactive conditions. Paired CK13 and CK17 immunohistochemistry shows promise in aiding dVIN diagnosis.

S-03-016
The immune checkpoints CTLA-4 and PD-L1 in carcinomas of the uterine cervix
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Objective: The aim is to investigate the expression of PD-L1 and CTLA-4 in carcinomas of the uterine cervix.
Method: 63 specimens of cervical cancerous and pre-cancerous lesions were immunohistochemically studied for the expression of PD-L1 and CTLA-4. They included 27 invasive adenocarcinomas, 19 invasive squamous cell carcinomas, 7 adenocarcinomas in situ and 10 high grade squamous intraepithelial lesions (CIN3).
Results: CTLA-4 tumour and immune cells expression was found in 61.5 and in 15.3 % of the invasive cases, respectively. PD-L1 tumour and immune cells expression was found in 26.9 and 19.2 % of the invasive cases, respectively. CTLA-4 tumour cells expression($p = 0.04$) and PD-L1 tumour($p < 0.0001$) and immune($p = 0.004$) cells expression were more often found in squamous cell carcinomas than adenocarcinomas .CTLA-4 tumour cells expression was correlated with FIGO stage ($p = 0.03$). Lymph node metastasis was more often associated with PD-L1 and CTLA-4 immune cells expression ($p = 0.03$, and = 0.06 respectively). Prognosis was dismal for PD-L1 expressing tumours ($p = 0.03$), but it was not associated with CTLA4 expression ($p = 0.6$).
Conclusion: CTLA-4 and PD-L1 are potential therapeutic targets in cervical cancer.

PS-03-017
Comparison of two cervicovaginal self-collection methods for detection of clinically significant human papillomavirus infection in Norwegian women
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Objective: Limited evidence is available on the performance and acceptability of different self-sampling devices. We compared two self-collection methods in Norway.
Method: 310 women referred to treatment for CIN 2+ completed self-collection using Evalyn Brush and FloqSwabs and filled a questionnaire. Self-specimens and a physician-specimen (reference) were tested for 14 high-risk HPV DNA using Anyplex, Cobas and GeneXpert. Agreement between self- and physician-specimens was assessed with kappa (κ). Sensitivities were compared using a matched-pair design.
Results: Analyses included 251 matched triplets. The hrHPV prevalence in the reference specimen was 89 % using Anyplex and 86 % using Cobas and GeneXpert. Agreement for hrHPV detection between self- and

physician-specimens ranged from 82 % with GeneXpert on FloqSwabs (κ = 0.47, 95 % CI: 0.35–0.59) to 94 % with Anyplex on Evalyn (κ = 0.68, 95 % CI: 0.53–0.83). Anyplex detected 95 % of CIN 2+ lesions, GeneXpert 94 % and Cobas 93 % on reference specimen. The sensitivity of any hrHPV test on Evalyn was similar to that of reference, significantly lower sensitivities were observed for FloqSwabs. Both devices were well accepted, women considered Evalyn easier, less painful and less uncomfortable than FloqSwabs.
Conclusion: We observed significant device effects on acceptability and performance to detect clinically significant hrHPV infection.

PS-03-018
p16/Ki67 test for triage women with histologic HSIL-risk in primary HPV-based cervical cancer screening
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Objective: HPV testing is adopted into cancer prevention systems by several countries as a primary method of screening. Effective triaging of HPV-positive women is substantial in detecting precancerous lesions. p16/Ki67 has been studied for indicating of high-grade cervical intraepithelial lesion risk by co-expression of anti-proliferative/proliferative markers. We investigated a diagnostic value of p16/Ki67 as the second-step in HPV-based screening.
Method: From 8350 screening tests (period 08/2015–03/2017) a group of 184 cases was selected based on 3 end-points: DNA HPV testing for 14 high-risk types, double immunocytochemical p16/Ki67 testing (DS) in cytopathologist diagnosis and following colposcopy with biopsy.
Results: Total number of histologic HSIL/DS positivity was 33/30 (for positive 16 or 18 HPV type 21/20 and for positive non-16 or non-18 types 12/10), for histologic LSIL was 149/37 (for positive 16 or 18 HPV types 61/20 and for positive non-16 or non-18 types 86/15). Sensitivity/specificity/PPV/NPV of DS for hHSIL were 91/75/45/97 respectively. In retrospective analysis, total number of biopsies needed in p16/Ki67-based triage was 67 comparing to 184 in LBC-based triage.
Conclusion: p16/Ki67 can be a useful diagnostic tool for detecting hHSIL in HPV-positive women and may reduce number of biopsies and increase patients comfort. In consequence, it could reduce costs of secondary screening.

PS-03-019
Mismatch repair deficient gland foci in histologically normal endometrium of Lynch syndrome patients
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Objective: While screening prophylactic gynaecological specimens of Lynch syndrome (LS) patients, we observed mismatch repair deficient gland foci (MMR-DGF) in normal endometrium. Therefore, we aimed to comprehensively analyse the presence of MMR-DGF in normal endometrium of LS patients.
Method: Normal endometrium from LS patients with (n = 3) and without adjacent cancer (n = 71), were analysed for MMR-protein expression by immunohistochemistry. The control group consisted of normal endometrium from non-LS patients. MMR-DGF were defined as histologically normal endometrial glands with uni- or multifocal loss of MMR-protein expression.
Results: MMR-DGF were present in 39 % (29/74: MSH2(14/26), MSH6(12/28), MLH1(2/24) and PMS2(1/3)) of LS patients, and were absent in all controls. In a subset of cases (n = 11), which were totally submitted, a much higher frequency was observed (64 %, 7/11). The protein loss corresponded with the gene affected by the germline variant. MMR-DGF varied in size (1to >40 glands/foci) and were frequently multifocal (71 %, 20/28).
Conclusion: This is the first comprehensive description of MMR-DGF in morphologic normal endometrium of LS patients. The prevalence of endometrial cancer in LS is much lower than the occurrence of MMR-DGF, indicating not all MMR-DGF develop into endometrial carcinoma. Pathologists should be aware of these lesions and not misinterpret these as neoplastic.

PS-03-020
Fumarate hydratase deficient uterine leiomyomas: A case report in Omani patient
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Objective: Identification of HLRCC patients presenting first with uterine leiomyomas may allow early intervention for renal cell carcinoma.
Method: A 42-year-old female presented with menorrhagia due to multiple uterine leiomyomas.
Results: Hysterectomy was done and the specimen was sent for histopathology. Gross examination revealed multiple subserosal, intramural and submucosal oval shaped white firm masses measuring from 0.3 to 7.7 cm in diameter. Microscopy showed well-circumscribed neoplasms composed of interlacing fascicles of smooth muscle fibers with rare mitoses of 0–1/10 hpf. Many of the nodules showed increased cellularity and diffuse cellular atypia with cells having large hyperchromatic nuclei with few scattered multinucleated giant cells. In some areas the cells exhibit prominent cytoplasmic eosinophilia and the nuclei showed perinucleolar clearing of the chromatin. Dilated staghorn-like vessels were seen. No coagulative necrosis was seen. immunohistochemistry showed complete loss of fumarate hydratase in the tumour cells and retained expression in endothelial cells and normal myometrium.
Conclusion: FH immunostaining should be performed on leiomyomas with features suspicious for FH-deficiency. If an FH-deficient uterine leiomyoma is diagnosed, the possibility of HLRCC should be considered clinically, particularly in young age. Careful clinical history and family history and eventual genetic counseling should be recommended.

PS-03-021
Endometriosis and carcinogenesis
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Objective: Endometriosis is a puzzling disorder characterized by the presence of tissue resembling endometrium outside of its normal position lining the uterus. There are many theories that can not elucidate the formation of this disease, even the most accepted "Retrograde Theory" is inadequate to explain endometriosis in non-pelvic tissues. In the light of these deficiencies of the theories, similarities between pathogenesis and metastatic pathways were tried to be explained by examining gene expressions in this study.
Method: From the National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO) database, datasets for genes with normal endometrium and endometriosis were analyzed by bioinformatic analysis using the R statistics software. A p value less than 0.05 was considered statistically significant.
Results: As a result of the investigations, statistically significant differences were observed in the expression of the genes that may be related to

the metastatic pathways, such as intravasation, escape from immune system, extravasation, proliferation, angiogenesis in patients with endometriosis.
Conclusion: It was concluded that a metastatic pathway could be used for the formation of endometriosis and this formation might be precancerous. It is aimed that precancerous endometriosis will be a guide in the production of anticancer drugs by giving a new dimension to endometrial cancer researches.

PS-03-022
Can Metallothionein and HSP-70 indicate placenta intoxication by tobacco smoke?
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Objective: Macroscopic placenta features and neonatal elements of infants born at term do not show sufficient variations on which to rely in determining exposure to tobacco smoke during pregnancy. The aim of this study is to determine whether Methalothionein and HSP-70 can distinguish infants exposed to tobacco smoke.
Method: 290 postpartum women were divided into four groups with respect to the smoking habit: NS, non-smokers, PS, passive smokers; AS, active smokers; APS, both partners active smokers. Immunohistochemical analysis with Metallothionein and HSP-70 was performed in order to obtain PIHI (placental immunohistochemical index). Statistical analysis was used to compare differences in the level of intoxication among groups, and correlation with the number of cigarettes smoked.
Results: PIHI showed a significant difference between group NS and the other groups, but not among groups AP, SP and HP. PIHI and both Metallothinein and HSP-70 showed a positive correlation with the number of cigarettes smoked.
Conclusion: PIHI can distinguish placentas exposed to tobacco smoke, but not the mode of exposure (passive vs. active vs. combination). Based on the results of the study, Metallothionein and HSP-70 can be used on every day basis as practical indicators of intoxication of placenta by tobacco smoke.

PS-03-023
Treatment practices for cervical intraepithelial neoplasia (CIN) in The Netherlands: Do they reflect the new guidelines for treatment of CIN?
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Objective: To compare trends in pathology data with new Dutch treatment guidelines for CIN to define areas requiring further guideline implementation.
Method: Using data from the Dutch Pathology database (PALGA) from 1 January 2005 to 31 December 2014, diagnoses and treatments between referral and the next primary screening round were ranked to identify the most severe diagnosis and most invasive treatment. Only cases with CIN as the most severe diagnosis were included for analysis.
Results: The proportion of women with CIN 1 treated with excisional techniques increased with age and referral type and ranged from 16.7to 50.4 %. On average, seven out of 10 women diagnosed with CIN 2 were treated with excisional techniques with no variation by age. See-and-treat management was more commonly used in women with CIN 2+ lesions, ranging from 14.6 to 25.9 % (varying by referral type and severity of diagnosis).
Conclusion: The rates of excisional treatment for CIN 1 lesions were not in line with current treatment guidelines. Offering see-and-treat management for women diagnosed with CIN 3 and allowing for watchful follow-up for CIN 2 in younger women are areas of clinical practice that should be improved to meet the new guidelines.

PS-03-024
Expression of paired box gene 8 (PAX8) in mesothelial cells
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Objective: It is critical to distinguish mesothelial cells from Müllerian neoplastic cells in peritoneal fluids or peritoneal biopsies for clinical staging of ovarian tumours. Transcription factor PAX8 has been widely used as a sensitive and reliable marker for distinction in both cytology specimens or in surgical pathology specimens. However, whether there is a gender difference in the expression of this marker in mesothelia or if reactive status affects its expression has not yet been well evaluated. The goal of this study is to examine whether mesothelium is immunopositive for PAX8 in some settings, which may cause diagnostic problems in difficult cases.
Method: Immunochemistry was carried out using PAX8 antibody on archival tissue from 50 peritoneum (25 women and 25 men) with either inactive mesothelia or reactive mesothelial cells and nuclear reactivity in more than 5 % of cells was considered positive.
Results: Twenty percent (10/50) of the cases were focally positive for PAX8, especially in reactive mesothelia (7/10) of female patients (9/10).
Conclusion: Reactive mesothelial cells of female patients tend to have focal immunoreactivity for PAX8, which may cause a diagnostic pitfall, especially in small biopsies or cytological specimens. Cautious interpretation of the positive immunostaining is essential to reach the correct diagnosis.

PS-03-025
Biovular and binucleated follicles occurrence in autologous ovarian tissue transplantation for fertility preservation
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Objective: Biovular and binucleated follicles have been described in rare human primordial and maturing follicles. Their occurrence and clinical significance are poorly understood. Recently, an association between biovular follicles occurrence and chemotherapy has been suggested. Our objective was to evaluate the incidence of biovular follicles in ovaries resected for autologous ovarian tissue transplantation performed for fertility preservation and examine their association with chemotherapy and age.
Method: A cohort of 100 ovarian tissue samples was histologically evaluated in multiple sections for the occurrence of biovular follicle. Tissue samples were of both recently resected ovaries destined for cryopreservation as well as thawed cryopreserved ovaries planed for up-coming transplantation. Clinical data regarding chemotherapy was retrieved.
Results: Out of 100 samples, 8 ovaries contained isolated biovular follicles. Only 2 of these ovaries were resected after chemotherapy administration. Whereas patient age for the entire cohort ranged from 2 to 45 years, patients with isolated biovular follicles were significantly younger (average age: biovular follicles 21.8 years vs. single-ovular follicles 32.1 years, p-value = 0.005 in two-tailed T-test).
Conclusion: In our cohort, biovular follicles were found in 8 % of the patients, their occurrence did not correlate with administration of chemotherapy, but appeared in younger patients, mostly adolescents.

PS-03-027
The utility of ThinPrep cytology and immuno-histochemical staining of p16 (INK4a), Ki-67 and P63 in assessment of cervical intraepithelial neoplasia (Dysplasia)
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Objective: The aim of this study was to compare and evaluate the results of both ThinPrep Pap cytology and immunohistochemical staining

pattern of p16, Ki-67 and p63 in diagnosing and grading cervical dysplasia in order to increase the diagnostic accuracy in equivocal cases.
Method: The present study was carried on 38 cases with non-dysplastic and neoplastic cervical lesions; initial screening with ThinPrep cytology was performed. Immunohistochemical staining of p16, Ki-67 and p63 was performed for all cases. The results were compared with histopathological diagnosis.
Results: ThinPrep cytology was found to have 100 % sensitivity in detecting low and high grade squamous intraepithelial lesions with relative low specificity when compared with confirmed histopathological results. Diffuse strong band-like p16 immunostaining was detected in 71.4 % CIN2, 91.7 % CIN3 and 87.5 % SCC cases with significant association with CIN grade ($p < 0.001$). Most of CIN3 and SCC cases showed strong Ki-67 and p63 expressions with significant CIN grade association ($p < 0.001$ for both). A significant positive correlation was found between the three biomarkers expression.
Conclusion: ThinPrep cytology with a slightly high sensitivity could be useful as screening method to detect squamous intraepithelial neoplasia and squamous cell carcinoma cases. Also, p16 and Ki-67 are valuable diagnostic markers for cervical lesions, and the expres¬sion level of p16, Ki-67 and p63 increase as the cer¬vical lesion is higher. Thus combined staining of these three studied biomarkers is useful for detecting and grading CIN especially in problematic cases for optimum management.

PS-03-028
Morphological base of pelvic pain syndrome in deep endometriosis
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Objective: Endometriosis (EM), which is an abnormal appearance of endometrial tissue outside of uterus, has chronic pelvic pain as one of the core clinical manifestations and poses a major challenge for the health care system. Aim of the study: to examine morphology and neural tissue markers in endometriosis lesions of various anatomic localisations in women with and without pain syndrome.
Method: We studied surgical samples (colon, urinary bladder, rectovaginal septum, peritoneum of the lower pelvis) from 52 patients diagnosed with either «pain-free» variant of EM (cohort #1) or EM accompanied with pain syndrome (cohort #2). Tissue sections from paraffin-embedded samples were subjected to immunohistochemistry via standard protocols with the following primary antibodies: PGP 9.5; NF (clone 2 F1); NGF (clone E-12); NGFRp-75 (all – from Dako, Denmark).
Results: chronic inflammation, per neural type of growth, neuromas development in foci of EM and remodeling of nerve fibers and neural endings in endometriosis lesions, with PGP 9.5, NGF and NGFRp-75 involved in formation of new nerve fibers result in formation of chronic pain syndrome in EM.
Conclusion: Morphological characteristics and immunohistochemical phenotype of EM lesions was independent of their anatomic localisation but showed good correlation with pain status of the patients.

PS-03-029
622 cases of cervical HPV gene screening and the characteristics of classification and distribution of positive-HPV infection
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Objective: To investigate the characteristics of classification and distribution of HPV infection, we explored the Gene expression of HPV via gene testing 622 cases cervical specimen submitted by Maternal and Child Health Hospital of Decheng district, leading to establish the analytical epidemiological characteristics of HPV in Dezhou city.
Method: A series of 622 patients who had cervicovaginal samples for HPV testing was selected between February 2014 and April 2015. The statistical analysis of infection of subtype HPV and age distribution were conducted on patients who were tested positive for HPV genotyping.
Results: 622 women were invited to participate in the HPV gene screening, 144 samples tested positive for HPV-infected (23.15 %). Most positive-HPV infections were high risk HPV (85.42 %). And the top 5 subtypes of high risk HPV were HPV 16, 58, 52, 31 and 18 with the proportion of 62.92 % of high risk HPV. For the low risk HPV, HPV 11 and 6 were the primary subtypes, which accounted for 95 % of the low risk HPV. The positive rate of total HPV, high-risk and low-risk HPV infection were statistically difference in a regrouped age groups (under 30, 30–60, over 60-years-old, respectively) ($P < 0.05$).
Conclusion: In summary, the genotyping test exhibited that infection rate of female cervical HPV infection was 23.15 % in Dezhou city, in which primary subtypes of high risk HPV (16, 58, 52, 31 and 18) and low risk HPV (11 and 6) were evidenced. In addition, the infection rate was peak in the group of under 30 years-old and reduced in an age-dependent manner.

PS-03-030
Teratoma with malignant transformation: Review of three cases
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Objective: Teratomas are the commonest primary ovarian tumour neoplasm. In the last 4 years our Pathology department received around 420 new cases of teratomas in women aged 14–83, most of them were mature teratomas. There were 14 cases of struma ovarii among them. Malignant transformation of mature teratomas and struma ovarii is rare and occurs usually in postmenopausal women.
Method: We present three cases of malignant transformation, one of carcinoid tumour arising in a mature teratoma and two cases arising in a struma ovarii, one follicular and the other papillary carcinoma.
Results: All three cases occurred in postmenopausal women with a mean age of 59 years. The follicular carcinoma had already metastasized to the pouch of Douglas upon diagnosis.
Conclusion: Carcinoid tumours, arising in mature teratoma, occurs in 1 % of all carcinoid tumours and malignant transformation of struma ovarii can be found in 5–10 %. Malignant struma ovarii represents only 0.01 % of ovarian tumours.

PS-03-031
Utility of immunohistochemistry in evaluation of microsatellite instability in endometrial carcinoma
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Objective: The mismatch repair (MMR) system is a strand-specific DNA repair mechanism. MMR deficiency results from germline mutations of MLH1, MSH2, MSH6, and PMS2 or from hypermethylation of MLH1 promoter. Endometrial cancer (EC) of MSI phenotype accounts for 22–35 % of all endometrial cancers. Identification of possible MMR mutation is made either by molecular analyses and/or immunohistochemistry. The aim of this study was To evaluate the immunohistochemistry profile and to assess its utility in detecting MSI in EC
Method: We enrolled 54 patients with EC diagnosed at Salah Azaeiz institute at Tunis, (2012–2016). immunohistochemistry for MLH1, MSH2, MSH6, and PMS2 was performed. We analyzed: expression of

MMR-Protrein (intensity, percentage), age, morphologic characteristics at diagnosis.
Results: The mean age was 58,6 years. Histologic subtypes were EC type I in 82 %, EC type II in 11 % and carcinosarcoma in 7 %. 12 patients (14.5 %) were younger than 50 years. Ten patients had altered expression of at least 1 MMR-P (22,2 %). Eight patients had a deficit of MLH1/PMS2 (15 %), 2 of PMS2, 1 of MSH2/MSH6, and 1 of MSH6. The intensity of the staining was at least moderate for the four MMR-proteins in more than 65 % of the cases. The percentage of positive cells varied between 79 and 100 % depending on the markers.
Conclusion: Immunohistochemical MMR status analysis in endometrial carcinoma may be an important adjunct when screening for hereditary cases.

PS-03-033
Histologic pattern of abnormal uterine bleeding in endometrial curetting in Lagos University Teaching Hospital in 2015
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Objective: Abnormal uterine bleeding (AUB) is a common presenting complains in the gyneacological out-patient department. Histopathologic evaluation of endometrial curettings play an important role in diagnosing these cases. The aim of this study is to determine the histopathologic spectrum of endometrial curettings in women with AUB submitted to the Department of Anatomic and Molecular Pathology, LUTH from January to December 2015.
Method: Histopathology reports of women with abnormal uterine bleeding were retrieved from the departmental archives. The diagnoses were categorized and analyzed.
Results: : Fifty four curettings performed for AUB were seen during the study period. The age range was 22 to 77 years. Most cases(63 %) were seen in the perimenopausal period (40s to 50s). Non-atypical hyperplasias accounted for the majority (33.3 %). This was followed by endometrial polyps (24.1 %), endometrial malignancies (22.2 %), stromoglandular differentiation (5.6 %), normal endometrium (5.6 %).Endometritis was seen most commonly in the 30s while malignant neoplasms peaked in the 60s. Normal endometrium, endometrial hyperplasias, polyps and stromo-glandular dissociation were seen most commonly in the perimenopausal period.
Conclusion: : Histopathologic examination of endometrial curettings reveals a wide spectrum of changes especially in the perimenopausal period. Histologic examination is especially warranted in this age group.

PS-03-034
Increased expression of cyclooxygenase-2 in nodular and diffuse adenomyosis uteri
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Objective: Comparative evaluation of cyclooxygenase-2 (COX-2) expression at areas of nodular and diffuse adenomyosis.
Method: By immunohistochemical methods, detected COX-2 (1: 200, Invitrogen) in the areas of eutopic and entopic endometrium of patients operated on for nodular (n =15) and diffuse (n =17) adenomyosis uteri. A quantitative estimate of the immunohistochemical reaction intensity in the cytoplasm of epithelial and stromal cells was estimated by means of Nikon Eclipse microscope imaging software (NIS-Elements).
Results: In the preparations of the eutopic endometrium, the highest level of expression was observed in the cytoplasm of epithelial cells in the proliferative phase, significantly exceeding the corresponding values of stromal cells at 1.9 times larger ($p < 0.05$). In secretion phase, COX-2 expression in the epithelial cells also prevailed, but only by 9.7 %. The highest values of COX-2 registered in nodular adenomyosis. The levels of COX-2 in the cytoplasm of epithelial and stromal cells nodular adenomyosis exceeds corresponding endometrial parameters in the proliferation phase by 143.1 and 91.8 %, respectively ($p < 0.05$), and in diffuse adenomyosis by 128.5 and 30,1 % respectively.
Conclusion: Adenomyosis uteri, especially nodal, characterized by higher levels of COX-2 expression compared to eutopic endometrium, which may be the basis for the development of targeted therapies.

PS-03-035
Molecular mechanisms and morphology of leiomyoma reduction induced by selective progesterone receptors modulators
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Objective: To study molecular mechanisms and morphological substrate of leiomyoma reduction in reproductive-age patients, receiving a selective progesterone receptor modulator (SPRM) for 3 months.
Method: The study was performed on leiomyoma taken during laparoscopic myomectomy from 75 reproductive-age women with uterine myoma, accompanied by menorrhagia and anemia. 40 patients underwent surgery after 3 month SRPM treatment (group I) and 35 patients underwent surgery only (group II). Morphological and immunohistochemical analysis (SRC-1, NCoR-1, ER, PgR, Ki-67, p16, TGF-β, VEGF) were made.
Results: In group I excessive bleeding stopped after 4–7 days from start of treatment, ultrasound revealed decrease in fibroid size ($p < 0,05$), Hb level increased ($p < 0,01$). The morphological substrate of leiomyoma reduction in I group were apoptosis and dystrophic changes of leiomyocytes, sclerosis and hyalinosis of tumour stroma and vessel walls sclerosis, with low ki-67 and p16 increase, low VEGF and TGF-β and hormonal reception dysregulation revealed in low SRC-1 expression with unchanged levels of NCoR-1, ER, PR.
Conclusion: Molecular mechanisms of tumour reduction included SRC-1, Ki-67, VEGF and TGF-β decrease and p16 increase in smooth muscle cells, with unchanged levels of PR, ER and NCoR-1. Obtained results show increase in apoptosis, decrease in proliferation and angiogenesis as a morphological base of leiomyoma reduction.

PS-03-036
May lymphadenectomy be removed in granulosa cell tumours of the ovary?
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Objective: To evaluate the usufulness of lymph node dissection in the management of patients with ovarian granulosa cell tumours.
Method: At Salah Azeiz institution, we conducted a retrospective chart review of all patients with ovarian granulosa cell tumours from January 2001 to July 2016.
Results: We identified 81 patients with a median age of 49 years (range, 7–96 years). Sixty-eight (68 %) were incompletely surgically staged at diagnosis due to the absence of pelvic and/or aortic lymph node dissection. Only13 patients had a lymph node dissection. Lymph node sampling was either pelvic and/or paraaortic. The median number of pelvic lymph nodes removed was 18 (range, 0–48 nodes). The median number of paraaortic lymph nodes removed was 4 (nodes; range, 0–19 nodes). Among these 13 cases, 11 (85 %) patients had adult type and 2 (15 %) had juvenile histology. Only in 2 cases, lymph nodes metastases were seen. The first case was adult type and the second case was juvenile histology. In these cases, metastases were observed in one lymph node.
Conclusion: Complete surgical staging was performed in approximately 1/6 women with ovarian granulosa cell tumours. However, 2 cases of

nodal metastasis were identified which confirmed the importance of lymphadenomectomy in such tumours.

PS-03-037

P16 patchy staining pattern in cervical biopsies. Should it be always interpreted as negative?

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Objective: Immunostaining with p16 helps in the histological diagnosis of cervical squamous lesions. It is considered positive when a strong and diffuse stain is present, and negative when there is no immunostaining or a focal/patchy pattern is observed. AIM: To determine if the patchy staining pattern must be always considered as negative
Method: 10 biopsy cases were identified with a p16 patchy/focal immunostaining pattern. 9 of them were L-SIL (CIN-I), and one H-SIL (CIN-II). HPV test was performed in the biopsy. Evaluation of the results, background and follow-up was recorded.
Results: Previous cytological diagnosis:7 L-SILHPV-HR+; 1 ASCUS HPV-HR+, 1 negative HPV negative, and 1 H-SIL HPV-HR undetermined. Follow-Ups: out of the 7 LSIL cases, 3 were HPV-HR determined and developed 1 H-SIL, 1 L-SIL, and 1 was free of lesion. Three other cases were negative for HPV in the biopsy, and only one developed a L-SIL, the two others had no lesion. The case determined as HPV-LR (Low Risk), and in the follow-up developed a L-SIL. The ASCUS HPV positive case confirmed in the biopsy as a HPV-HR was lost to follow-up.
Conclusion: The focal/patchy p16 immunostaining pattern cannot exclude the progression of the lesion to H-SIL.

PS-03-038

Small cell neuroendocrine carcinoma of the uterus: A case report and review of the literature

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Objective: Primary small cell neuroendocrine carcinoma (SCC) is extremely rare entity with 80 cases reported. It is an aggressive tumour with poor prognosis. There is no sufficient data about its treatment.
Method: We report a case of 52-year woman with a diagnosis of primary small cell neuroendocrine carcinoma associated with endometrial adenocarcinoma G1 of the uterus. Patient underwent surgery.
Results: Macroscopically, the endometrium was replaced by tumour with areas of necrosis, with invasion of myometrium more than ½. Histologically tumour presented as sheets and nests of small-sized cells with hyperchromatic nuclei and scanty cytoplasm. There was synchronous grade 1 endometrioid adenocarcinoma of the uterus. Areas of necrosis were present. Multiple emboli in myometrium and cervix were found. Tumour cells were positive for synaptophysin and chromogranin A, MIB-1 expression was 90 %. CD10 was negative thus diagnosis of stromal sarcoma was excluded.
Conclusion: The diagnosis of small cell carcinoma of the uterus must be done only after rigorous pathological examination. Differential diagnosis should include metastatic small cell carcinoma, stromal sarcoma, mixed mullerian tumours.

PS-03-039

The clinicopathologic significance of the ARID1A expression in ovarian epithelial tumours

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Objective: AT-rich interactive domain 1A (ARID1A) or BAF250a protein, which is encoded by tumour suppressor ARID1A gene, involves in chromatin remodeling. Mutations in ARID1A gene are almost always associated with loss of protein expression as assessed by immunohistochemistry. The aim of this study is to investigate the association between tissue ARID1A expression and the clinicopathologic features of ovarian epithelial tumours.
Method: The resection specimens of 137 patients who were diagnosed and treated in Izmir Tepecik Education and Research Hospital between 2002 and 2013 were included in this study. ARID1A expression was studied in a total of 137 formalin-fixed, paraffin-embedded specimen of ovarian epithelial tumours.
Results: In this series, there were 89 ovarian epithelial carcinomas, 12 borderline, and 36 benign serous ovarian tumours. Among malignant tumours, 34 serous, 17 mucinous, and 38 endometrioid carcinomas were detected. Statistically it was determined that the expression of ARID1A was significantly lower in benign serous tumours when compared with borderline serous tumours and serous carcinomas ($p < 0.001$). Contrary to serous carcinoma, the decreased levels of ARID1A expression were found in endometrioid and mucinous carcinomas (0.033).
Conclusion: Our findings demonstrated the presence of a correlation between ARID1A expression and the pathogenesis of both mucinous and endometrioid carcinomas. However contrary to previous studies, ARID1A expression was not downregulated in borderline serous tumours. Therefore we suspected that borderline serous tumours may be more closely related to high grade serous carcinoma than benign serous tumour.

PS-03-040

Mechanisms of development of large leiomyomas

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Objective: Large leiomyomas (LL) of the uterus are characterized by increasing of the uterus due to myomatous nodes up to the size of a 12 week pregnancy and more. The aim was tostudy mechanisms of LL development based on immunohistochemical (IHC) studies of Ki67, TGFβ, CD117, PD-ECGF, connexin and nestin.
Method: biopsy and postoperative material of 54 patients with simple tipe leiomyomas were analized. Patients were divided into two groups with LL and control with leiomyomas, less than 4 cm in diameter. Each group was divided into two subgroups by age: women younger than 45 years and women over 45 years. Immunohistochemistry (IHC) determined the expression of Ki67, TGFβ, CD117, PD-ECGF, connexin and nestin.
Results: IHC showed increased expression of Ki-67, PD-ECGF, TGFβ in growth zones in LL in comparison with small leiomyomas, especially in women over 45 years of age.
Conclusion: Pathogenetic mechanisms of growth of LL are associated with activation of stem and progenitor cells in the perivascular regions of LL growth, which is manifested in the enhancement of expression of the stem markers TGFβ, CD117, PD-ECGF, Ki67, connexin and nestin in the cells of their genera. The most pronounced activity of growth zones by molecular markers is found in women with leiomyomas larger than 45 years, which requires oncological alertness.

PS-03-041

Signaling molecules as markers of endometrial receptivity: Ways of targeted therapy optimisation

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Objective: Optimizing the efficiency of in vitro fertilization (IVF) is directly connected with the endometrium receptivity. Verification of key signaling molecules that ensure the ability of implantation makes it possible to assess the readiness of the endometrium for implantation. Aim of

study. To identify the markers of endometrial receptivity for optimization of targeted therapy of infertility.
Method: The study of endometrium's samples resulting in a period of "implantation window" for one cycle before treatment by confocal microscopy using antibodies to ER, PR, VEGF, TGF-beta1, integrin αVβ3, LIF was carried out. We evaluated the optical density (OD) and the expression square (S) of markers.
Results: IVF outcome prediction algorithm was designed for different patient groups. For women with male factor infertility are most important the expression of LIF, integrin αVβ3 and TGFβ1. For women with tubal-peritoneal factor infertility the most informative markers are LIF, integrin αVβ3 and PR/ER expression. For a group with external genital endometriosis important for prognosis are TGFβ1, VEGF-A, LIF, integrin αVβ3.
Conclusion: The study of molecular mechanisms of endometrial receptivity allows to choose the targeted therapy in order to increase the ability of endometrial implantation.

PS-03-042
Lymphoepithelioma-like carcinoma of the uterine cervix: Clinical and immunohistochemical study of 3 cases
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Objective: Lymphoepithelioma-like carcinoma is a variant of squamous cell carcinoma clinically associated with a good prognosis.
Method: We hereby report three cases of lymphoepithelioma-like carcinoma in the uterine cervix diagnosed within 3 years.
Results: The patients' mean age was 42.0 years. The cervical smear had shown ASCUS or HSIL and the initial cervical biopsy showed either high-grade cervical intraepithelial neoplasia (CIN3) or squamous cell carcinoma. All patients underwent a Wertheim operation, two of which were preceded by a cervicectomy. Microscopically, all tumours were characterized by poorly defined sheets of undifferentiated squamous cells with a syncytial pattern and a heavily lymphocyte-infiltrated background. On immunohistochemical analysis, the lymphocytes were predominantly CD3 and CD8 positive. The CD8-positive lymphocytes were the only ones found within tumour lobules. CD4-positive and CD20-positive lymphocytes were around tumour lobules. Scattered cells were positive for CD56 and CD79. An ISH staining for EBER was negative. All cases were positive for P16 by immunohistochemistry. Follow-up ranged from 2 months to 2,7 years and was disease-free in all three patients.
Conclusion: Lymphoepithelioma-like carcinoma of the uterine cervix is a variant of squamous cell carcinoma, known for its better prognosis. The high CD8-positive tumour infiltrating lymphocytes (TILs) can explain the good prognosis of this tumour.

PS-03-043
Immature teratoma: Review of five cases
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Objective: Immature teratoma represents only 1 % of ovarian cancer and 3 % of all teratomas. Since 2013 in our Pathology department we had 5 cases of immature teratoma among 120 cases of teratomas. Patients were of reproductive age, 16–38 year old. The average diameter of the tumours was 16 cm (11–24 cm). Three were solid and partially cystic and two were predominantly cystic.
Method: Sufficient sampling of the tumours was taken and a three tiered grading system was used. Foci of immature neuroepithelial tissue that occupy the low power field (40×) in each slide were measured. Foci of immature neuroepithelial tissue in one 40× field were designated as Grade 1, 1–3 fields Grade 2 and more than 3 fields Grade 3.
Results: One of the tumour was Grade 1,three of them were Grade 3 and one Grade 2 that occurred in the older patient, age 38.One of them had metastasis to the omentum with a coexisting mature teratoma in the other ovary and another tumour showed capsular invasion. All other cases were free of metastasis.
Conclusion: The grade and stage of immature mature teratoma along with grading of the implants are the predictive factor of the disease.

PS-03-044
Metastasis to the ovary as an initial manifestation of a primary tumour: Report of two cases
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Objective: Metastases to the ovary are very common most often from the colon, stomach and breast and are usually bilateral. They can mimic a primary ovarian tumour.
Method: We present two cases of metastatic cancers that were considered as primary ovarian carcinomas prior to surgery. Both women were of reproductive age and complained of abdominal pain. A U/S showed bilateral ovarian enlargement in the first case and enlargement in the right ovary in the second. Medical history was free.
Results: Frozen section diagnosis was of metastatic carcinoma in both cases. The final diagnosis in the first case was bilateral ovarian involvement by a squamous cell carcinoma of the cervix. A mass protruding from the cervix into the posterior uterus was seen on CT imaging. In the second case the diagnosis of an ovarian involvement by a pancreatic adenocarcinoma. A palpable mass was found in the pancreas following the frozen section diagnosis and diagnosis confirmed by immunohistochemistry (CK20, CDX2, MUC5A ,CK 17 positivity ,negative for CK7, ER)
Conclusion: Metastatic squamous carcinoma of the cervix to the ovary is very rare 1.3 %. In cases of ovarian involvement by pancreatic cancer the primary lesion is unsuspected at oophorectomy and will be usually discovered intra or post operatively.

PS-03-045
Diagnostic variation in p53 usage for endometrial carcinoma in biopsy or curetting specimens
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Objective: Retrospectively assess p53 usage in Endometrial Carcinoma (EC) biopsies.
Method: Malignant endometrial biopsies (June/15-December/16) were reviewed for WHO histotype and p53 status.
Results: Of 79 ECs, 74 % (59/79) were low-grade (LGEC = G1-G2 endometrioid EC) and 24 % (19/79) were high-grade (serous $n = 7$ and G3 EEC $n = 12$). 26/79 (33 %) biopsies had p53 performed, equating to 85 % (6/7) of serous histotypes, 83 % (10/12) of HGEC and 17 % (10/59) of LGEC. p53 mutations were present in 100 % (6/6) of serous, 22 % (2/9) of G3 EEC, and 20 % (2/10) of LGEC. The remaining 49 LGEC had p53 done on the resection ($n = 7$) or retrospectively on the biopsy ($n = 42$); all were wild-type.
Conclusion: In the ProMisE molecular classification, histotype integration could be beneficial when delineating Copy Number-High (CN-H) from Copy Number-Low (CN-L). Since 100 % of serous EC were mutated and the diagnosis was unaltered in the two mutated LGECs, a p53 is not warranted for clearly serous or LGEC histotype. Conversely, only 22 % of HGEC were mutated, making ancillary p53 testing the most

useful. Once MMR-D and POLE mutated carcinomas are classified, using LGEC and serous histotypes to assume CN-L and CN-H respectively may be suitable surrogates, leaving targeted p53 testing for HGEC/ambiguous carcinomas.

PS-03-046

Molecular features of uterus leiomyoma in reproductive-age women after previously performed inefficient Uterine Artery Embolisation (UAE), focused ultrasound ablation controlled by MRI (MRgFUS) and myomectomy

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Objective: to investigate the morphological, immunohistochemical features of uterus leiomyoma in reproductive-age women after previously performed UAE, MRgFUS ablation of fibroids and myomectomy.
Method: The study was performed on leiomyoma taken from 110 women 36,2 ± 5,2 years. Group I ($n = 32$) - patients with history of UAE, group II ($n = 26$) - patients after MRgFUS ablation and group III ($n = 52$) - patients, after myomectomy. The study included patients with ineffective treatment of fibroids. morphological and immunohistochemical investigation (VEGF, HIF-1, IGFR-1, Casp3, Ki67) was made.
Results: VEGF was high in group III, lower in group I and the lowest in group II. HIF-1 was significantly higher in group I (10.1 %) was moderate in group III (5.0 %); and it was very low in the group II (0.26 %), that was statistically significant, $p < 0.05$. In Group I, IGFR was 1.5 points; in group II-3,6 points; in group III - 2.7 points, $p < 0.05$. Ki 67 and Casp3 were low and comparable in all groups.
Conclusion: Obtained results show that in spite of different mechanisms of leiomyoma growth after inefficient initial treatment (UAE induces HIF-1 expression, MRgFUS may trigger growth through IGFR) the mechanisms of cell cycle regulation are preserved in all groups.

PS-03-047

The syndrome of undifferentiated Connective Tissue Dysplasia (uCTD) in a combination with Hereditary Thrombophilia (HT) as a cause of primary female infertility

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Objective: The combination of syndrome of uCTD and HT often accompany female infertility. The purpose was to study morphological and immunophenotypic features of the endometrium in patients with primary infertility in uCTD and HT.
Method: The study was performed on endometrial pipelle-biopsies taken in the "implantation window" from 81 patients with clinical diagnosis of uCTD (13 women), HT (40), with combination of uCTD and HT (19) and control group - healthy surrogate mothers (9). Morphological and histochemical study (hematoxylin and eosin, pikrofuksin by Van Gieson, toluidine blue) and immunohistochemical study with the antibodies to ER, PgR, LIF, PAI-1, VEGF, collagen I, collagen III, fibronectin, laminin, MMP-2, MMP-9 were performed on endometrial biopsy specimens.
Results: Main groups (uCTD, HT, uCTD + HT) showed signs of impaired endometrial receptivity: decrease of mature pinopodes level, retarding endometrial maturation, decrease of LIF, VEGF, and stromal progesterone and estrogen receptors expression and PAI-1 increase, compared to control. Foci of sclerosis in endometrial stroma in patient of main groups showed accumulation of collagen III, MMP2 and 9, fibronectin and laminin.
Conclusion: Obtained results show impaired endometrial receptivity in patients with uCTD, HT and especially with combination of these conditions. Endometrial stroma undergoes remodeling ending in stromal focal sclerosis, reduced endometrial receptivity and infertility.

PS-03-048

Expression of human epididymal secretory protein 4 may be a predictor for invasiveness in ovarian serous tumours

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Objective: Human epididymal secrotory protein 4 (HE 4), also known as WFDC2 , has a presumptive role in natural immunity. HE4 protein is originally described as an epididymis spesific protein but more recently suggested to be a putative serum tumour marker for ovarian cancer. The aim of this study was to investigate the association between tissue HE4 expression and the clinicopathological features of ovarian serous tumours.
Method: HE4 expression was studied in a total of 82 formalin-fixed , paraffin-embedded ovarian serous tumours specimens an its association with different clinicopathologic parameters was evaluated.
Results: In this series, there were 36 benign (43.9 %), 12 (14.6 %) borderline and 34 (41.5 %) malign serous tumours. Mean age of patients was 43.9 ± 14.4 years (17 to 72). In only 12 benign tumours (33.3 %), cytoplasmic HE4 expression was determined, while it was determined in 20 (58 %) serous carcinomas. In borderline tumours. the negativity and positivity rate of HE4 expressions are equal (n:6/50 %). Statistically it was determined if the tumour becomes more aggressive and invasive, it gains the HE4 expression ($p = 0.037$)
Conclusion: Our findings were demonstrated to link of HE4 expression and the aggresiveness of ovarian serous tumours. Therefore it may be suggested that the tissue expression of HE4 can be used to differentiate the borderline tumours from carcinomas.

PS-03-049

Teratomas of the ovary: A clinico-pathological evaluation of 247 patients from one institution during a 5-year period

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Objective: Mature cystic teratoma are the most common germ cell tumours of the ovary accounting for 10–20 % of all the ovarian tumours. They comprise approximately are third of all the benign ovarian neoplasm. Torsion, rupture and infection are more common complications of the mature cystic teratoma and only very rarely do these tumours undergo a malignant transformation.
Method: We analysed retrospectively the clinical and pathological characteristics of 242 mature cystic teratomas, 5 immature teratomas examined in our hospital during the last 5 years.
Results: The age range was from 4 to 80 years old. (median 36.2) The most frequent symptom was lower abdominal pain in 57 % of patients. A pregnancy was present 18 of patients. Bilaterality was present 12.1 % of patients. Tumour size ranged from 1.1 to 26 cm in diameter (median 8.1 cm) . The treatments consisted of cystectomy in 44.6 % of cases, oopherectomy in 29 % or hysterectomy with both adnexa in 26.4 % of cases. Malign changes with the teratomas were seen in 1.2 % cases. The operative video-laparoscopy was employed in 53 cases.
Conclusion: Mature cystic teratomas are the most common ovarian neoplasm, that occurs most commonly during the reproductive years. Malign transformation rate in these tumours is very low. We analysed our results and compared with the study

PS-03-050

Signet-ring like cells in an endometrial curetting, an incidental finding unveiling a metastatic disease to the ovary: A case report and review of the literature

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Objective: Metastatic disease to the ovary is one of the most common tumours in women. The mean age group is 55 years old (range: 26–78 years old) and the prevalence is 5 % of all ovarian neoplasms, in which tumours of unknown origin account for 14 % of the cases. The proportion of metastatic ovarian neoplasms varies according to the geographic region, ranging from 3 to 15 % in western countries, to 21–30 % in the eastern countries.
Method: Our case is of a 62 years old female, who presented with postmenopausal bleeding. Her endometrial curetting showed groups of signet-ring like cells, this initiated a battery of investigations and a subsequent hysterectomy. On histology, there was an extensive infiltration of signet-ring cell tumour involving ovaries, uterus and cervix. Immunohistochemistry pointed towards a gastrointestinal primary; however, both endoscopy, CT and PET scan failed to find a primary origin. The patient was eventually treated as a case of metastasis of an unknown primary.
Results: In a recently published study, data showed that metastasis to the ovaries can present before (18 %), synchronously (33 %) or after the primary neoplasm was identified. In those: 25 % were single, 40 % were unilateral and 47 % were ≥13 cm. Most originated from the gastrointestinal tract (73 %), followed by breast (13 %), and female reproductive organs (10 %). Gross features varied with primary tumour site.
Conclusion: Metastatic adenocarcinoma of unknown primary accounts for about 3–5 % of all the metastatic carcinomas. And in cases of ovarian tumours, metastatic disease should be always kept in mind and investigated, to avoid pitfalls in diagnosis and management.

PS-03-051
Malignant mixed mullerian tumour of the fallopian tube: Case report
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Objective: There are less than 80 cases reported in literature of Malignant Mixed Mullerian Tumours (MMMTs) of the fallopian tube and account less than 5 % of tubal malignancies and only a few cases reported in the fallopian fibriae.
Method: We report a case of a 74 year old female that was diagnosed with ovarian cancer on a cytological smear upon ascites. On CT scan a 6 cm right side mass was found. She underwent a 3-cycle chemotherapy and the mass shrunk sufficiently.
Results: A hysterectomy was performed with salpigoophorectomy, omentum removal and biopsies were taken from peritoneum, colon and the urinary bladder.Macroscopically both ovaries looked normal and on the right fallopian fibriae a 1,5 cm tumour was found. The omentum was full of macroscopical metastasis. The tumour on the right fallopian fibriae was biphasic. A serous adenocarcinoma with sarcomatous stroma elements and a heterologous malignant element consisted of cartilage were identified. Histological, both ovaries were normal. Metastases were found in all the biopsies that were taken.
Conclusion: A MMMTs of fallopian type can be diagnosed when a normal ovary is identified. In our case both ovaries were normal. MMMTs of the fallopian tube are aggressive neoplasm with increased mortality rate.

PS-03-052
Teratoid carcinosarcoma - an unknown neoplasm
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Objective: Teratoid carcinosarcoma is an extremely rare morphological variant of carcinosarcoma. The histogenesis is controverse and diagnosis can be difficult, due to the variegate morphology of epithelial and mesenchymal benign and malignant components; the presence of neuroepithelial areas is a characteristic feature. We report the findings of 3 pelvic cases.
Method: Stage III cases (1 ovarian bilateral), from 61, 72 and 86 years-old women, were analysed and the percentage of each component was recorded.
Results: All patients were submitted to surgery and 2 started chemotherapy, but all died from the disease (14 days, 7 and 12 months after the diagnosis). Tumours were 16,6 cm to 20 cm and the proportion of histological components in each tumour was variable. Endometrioid carcinoma was the most prevalent malignant epithelial component; however we also identify high-grade serous, mucinous and clear cell areas. Undifferentiated sarcoma was predominantly in all, but 2 cases had rhabdoid and chondroid areas. The germ cell component was yolk sac (most common) and neuroepithelial like-tubules within blastemal areas were focal to abundant.
Conclusion: Teratoid carcinosarcoma is an old women neoplasm with a wide variation of types and percentages of histological components. Further studies are needed to better understand cell neometaplasia and this dismal prognosis tumour.

PS-03-053
Clinicopathologic review of teratomas in Jos, North Central Nigeria
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Objective: To document and describe the clinical and pathologic features of teratomas diagnosed at the pathology department of the Jos University Teaching Hospital over a 10 year period.
Method: A retrospective hospital based study of all histopathologically diagnosed teratomas at the Jos University Teaching Hospital. Data regarding age, sex, site, clinical and histologic features were obtained from the records of the pathology unit of the Hospital. Teratomas were classed according to their histologic features using the World Health Organization (WHO) classification. Information obtained was depicted in the form of tables, and pie charts.
Results: 96 teratomas were diagnosed during the study period. Mean age was 27.4 years with 16.7 % of all cases seen in childhood . A male to female ratio of 1:15 was observed, females accounting for 93.8 % of cases. Gonadal teratomas were predominant,with extragonadal involvement seen in 16.7 % of cases.
Conclusion: Teratomas were commonest in children, indicative of the relatively higher number of totipotential cells in this age group as well as arrested migration of these cells during development.Occurrence of ovarian lesions as "incidentalomas" could be attributed to non specific symptoms and a retroperitoneal location.The presence of infertility is a consequence of destruction of functional ovarian tissue by the neoplasm.

PS-03-054
Is there any indication of Adamts-16 expression in endometrial polyps?
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Objective: Adamts, a metalloproteinase, plays a key role in the rearrangement of endometrial extracellular matrix. In this study, it was aimed to investigate the expression of Adamts 16 and relationship with age and menopausal status in endometrial polyps (EP).
Method: This study was conducted on a total of 72 paraffin-embedded EP samples, which were histopathologically diagnosed at the Department of Pathology of medicine Hospital between 2014 and 2015. Paraffin-embedded EP samples 3 μm in thickness, were then cut. The slides were

stained with Adamts 16. Gland and stromal cells were evaluated separately according to staining intensity.
Results: Statistically, it was determined that stromal staining results were changed according to gland staining results ($P < 0.001$). Stromal positive staining was observed in 93.1 % of cases with glandular positive staining. Statistically, it was determined that the results of Adamts16-gland staining did not change with age ($P = 0.180$). However, it was observed that stromal and glandular staining was more frequent in the over 45 year old group, clinically. Stromal staining in this group was 80.6 % (70.7 %, <45 years old) and glandular staining was 87.1 % (75.6 %, < 45 years old).
Conclusion: In this study, it was found that Adamts 16 expression tended to be co-stained in gland and stroma, and that there was more expression in the over 45 year-old group.

PS-03-055
Prognostic role of ER, PR, HER-2/neu expression in the fallopian tubes' cancer
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Objective: The aim of this study was to investigate of steroid receptors expression and the HER-2/neu oncoprotein in the tissue of the fallopian tubes' cancer.
Method: The protein expression was assessed by immunohistochemical analyses of 66 patients with serous adenocarcinoma of the fallopian tube.
Results: Cancer of the fallopian tubes more commonly affect the postmenopausal women, aged 60–69 years, mainly in early stages of the disease (I-II) (60.8 %) and in most cases is represented as serous adenocarcinoma (92.96 %). Most of them were ER-positive (83.33 %). The age does not influence the phenotype of the tumour. The study of the impact of differentiation grade on the tumour receptor phenotype showed the moderate negative correlation. Assessment of HER-2/neu expression showed the doubtful reaction in 9.1 % of cases ($n = 6$) that did not depend on the tumour differentiation grade, stage of disease and presence of metastases.
Conclusion: It was determined that most of them are receptor-positive for both steroid receptors and did not depend on the age. When the tumour differentiation grade becomes lower the number of receptors for steroid hormones also reduces. HER-2/neu expression is not typical for primary cancer of the fallopian tubes, taking into account almost complete lack of it in tumour tissue

PS-03-056
Pathology of the uterine cervix: Statistical data in Romania and Denmark, two very different countries in terms of screening programs
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Objective: The aim of this present study was to make a comparison of statistical data in the pathology of the uterin cervix in Romania and Denmark, two very different countries in terms of screening programs.
Method: We presents a retrospective study, where the data was collected from consecutive Pap smears from women who had been reffered to the gynecologist, from Arad, Romania and Viborg, Denmark. Samples was analyzed in the Pathology Departments of this two cities; both conventional smears and liquid-based cytology was performed.
Results: Our results show that the higher number of abnormal smears are in the patients aged 30–39 years in both analised lots, followed by age group 40–49 years. The high number of danish women under 30 years with abnormal smears (29,7 % of abnormal smears) draw the attention that also young women should be investigated and included in screening programs.
Conclusion: In the present study, we showed that there is a high prevalence of SCC (0,8 %) and precursor lesions (5,2 %) among romanian women, while in Denmark the prevalence of SCC is very low (0,1 %) and precursor lesions account for 7,3 % of all analised smears. Although, cervical cancer screening remain an evolving field with new HPV tests and development of new technologies, Pap smear tests remain a cheap and easy way to perform an effective and extensively population screening method.

PS-03-057
A coexistence case of primary fallopian tube carcinoma and ectopic pregnancy
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Objective: We report the case of a 34 year-old woman with primary fallopian tube carcinoma and ectopic pregnancy.
Method: The pathient presented abnormal vaginal bleeding and lower abdominal pain. Her medical history revealed one live birth and one spontaneous abortion in the first trimester. On examination, her vital signs were normal. A physical examination revealed right lower quadrant tenderness without rebound. Ultrasonography showed a complex right adnexal mass of 4.7 × 5.6 × 5.0 cm. Her human chorionic gonadotropin level was 305 IU/L. A provisional diagnosis of right tubal pregnancy was made and confirmed by subsequent laparoscopy. A total right salpingectomy was performed. Histopathological examination and immunohistochemistry tests were performed.
Results: Histapathological examination confirmed the existence of a tubal pregnancy. A well differentiated adenocarcinoma was an incidental finding in the same fallopian tube. The tubal mucosa and tubal wall was involved. Immunohistochemistry results of the tumour specimen: cytokeratin 7 positive, WT1 positive, PAX8 positive, cytokeratin 20 negative, CDX2 negative, villin negative. Metastatic colonic adenocarcinoma was excluded. No sign of primary tumour of cervix, uterus or ovary was found.
Conclusion: We report the extremely rare case of primary fallopian tube carcinoma, coinciding with an ectopic pregnancy.

PS-03-058
Signet-ring mucinous primary carcinoma of the ovary: Three cases in young women with detailed immunohistochemical and molecular analysis and clinical follow-up
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Objective: To present three cases of primary ovarian mucinous carcinoma with signet-ring cells in three young women (33–35 years old), with detailed immunohistochemical and molecular analysis and clinical follow-up.
Method:
Results: Two patients directly underwent to hysteroannessiectomy followed by adjuvant chemotherapy while the third one received neoadjuvant chemotherapy followed by surgery. Gastrointestinal endoscopy was negative in all patients. Due to very short disease-free interval, further treatments were started without substantial response in all patients. Histopathological examination revealed a mucinous carcinoma, with a predominant component of signet-ring cells and focal neuroendocrine features, involving both ovaries with loco-regional spread. Immunohistochemical analyses showed positivity for Keratins (pankeratin, CK7 ,CK19, CK20), E-cadherin, EMA and CDX-2, and

focal staining for p16, calretinin and neuroendocrine markers. All the other markers tested (HER2, vimentin, 1A4, desmin , CA125, WT1,CD99, Inhibin, p53, beta-catenin, villin, PAX8, hormone receptors) were negative. Neither BRCA1/2 (1 case) nor CDH1 (E-cadherin) pathogenetic mutations were identified. A single rs16260 regulatory polymorphism at the CDH1 promoter, leading to different transcriptional activity, was identified.
Conclusion: The distinction between primary and metastatic ovarian signet-ring carcinoma (especially from gastrointestinal tract) may be problematic, mainly due to overlapping immunophenotypes, and has important therapeutic implications. Clinical data are essential for the correct diagnosis.

PS-03-059
Adenosarcoma of the uterus: A case report
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Objective: Adenosarcomas are uncommon biphasic neoplasms of low malignant potential consisting of benign or atypical epithelium and a sarcomatous component. They occur usually in postmenopausal women and account for 0,4 % of all uterine cancers.
Method: We present a case of a 50 year old premenopausal patient with free medical history that presented with abnormal vaginal bleeding. A curettage was performed, a diagnosis of carcinosarcoma was made and a total abdominal hysterectomy with salpingoophorectomy followed. A single rubbery polypoid lesion was found in the endometrial cavity measuring 7,5 × 5 × 3 cm. The omentum and 67 pelvic lymph nodes were removed also.
Results: Histologically the tumour had a phyllodes-like architecture and the epithelial component was benign. The stromal component was low grade and was composed of spindled cells with low mitotic activity. Stromal type cells, CD10 positive, seemed to condensate around glands. A heterologous stromal element was also seen consisting of rhabdomyoblasts (sarcomeric positive).Superficial invasion of the myometrium was seen.
Conclusion: As adenosarcomas are more common the body of uterus and are usually misdiagnosed upon curettage, a surgical specimen is needed for the correct diagnosis. Patients with adenosarcoma have a good prognosis when the tumour is confined to endometrium

PS-03-060
Metabolomic and lipidomic profiling identifies the role of the RNA editing pathway in endometrial carcinogenesis
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Objective: Endometrial cancer (EC) remains the most common malignancy of the genital tract among women in developed countries. Despite concerted research efforts, there is a significant gap in the understanding of underlying mechanisms of disease progression.
Method: We used a high resolution mass spectrometry based molecular phenotyping approach to characterize metabolic profiles of 39 human EC and 17 healthy endometrial tissue samples and to gain insights into altered metabolic pathways in EC carcinogenesis. The dysregulation of the RNA editing pathway was further investigated and confirmed using an independent set of 183 human EC tissues and matched controls. In vitro assays were performed to characterize ADARs in endometrial carcinogenesis.
Results: We observed a dysregulation of several lipid pathways and the RNA editing pathway. We found that ADAR2 is overexpressed in EC in a manner that correlates with the tumour histological type and grade. Furthermore, silencing of ADAR2 in 3 EC cell lines (HEC-1A, RL95-2 and Ishikawa) resulted in a decreased proliferation rate, increased apoptosis and reduced migration capabilities in vitro.
Conclusion: Our results suggest that ADAR2 functions as an oncogene in endometrial carcinogenesis and could be a potential target for improving EC treatment strategies.

PS-03-061
Validation of a mitotic index cutoff as a prognostic marker in undifferentiated uterine sarcomas
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Objective: Undifferentiated uterine sarcomas (UUS) are a heterogenous group of high-grade mesenchymal tumours. A previous study demonstrated that a mitotic index cut off of 25 mitoses/10 high power fields (corresponding to 11.16 mitotic figures/mm2) could successfully divide these tumours into two prognostic groups with significantly different overall survival. The goal of the current study was to 1) validate this mitotic index cut off in an independent, multicenter cohort and 2) explore the prognostic value of mitotic index group in relation to other clinicopathologic variables.
Method: Cases were included from three independent institutions: The Norwegian Radium Hospital, The Mayo Clinic and Skåne University Hospital. A total of 40 tumours were included after central review. Molecular testing for the YWHAE-FAM22A/B and JAZF1-JJAZ1 translocations was performed on all cases. Survival data was available on all patients.
Results: The crude Cox Proportional Hazards model revealed a number of parameters that significantly impacted overall survival, including mitotic index group, patient age, stage, and the presence of tumour necrosis. Combining these parameters into an adjusted model revealed that only mitotic index group and stage were prognostic.
Conclusion: On the basis of these findings, it is proposed that UUS can be subdivided into "mitogenic" and "not otherwise specified" (NOS) types.

PS-03-062
Twin placenta with complete hydatidiform mole: Clinicopathological and immunohistochemical studies
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Objective: To clarify clinicopathological and immunohistochemical features of twin placentas with complete hydatidiform mole (CM)
Method: Twelve cases of twin pregnancies with CM in the first trimester and 3 cases of clinically putative twin pregnancies with CM were investigated by immunostaining p57 (Kip2) (p57) and TSSC3, which are products of paternally-imprinted, maternally-expressed genes.
Results: On histologic review, 12 cases were histologically diagnosed as CM with twins (a twin pregnancy with a coexisting normal placenta and CM). The admixture of large hydropic villi with circumscribed trophoblastic hyperplasia and smaller, normal-appearing villi without trophoblastic hyperplasia was observed in all cases. The cytotrophoblasts and stromal cells in the larger villi were negative for p57 (androgenic) and TSCC3, whereas these cells were positive in the smaller villi (biparental). Two cases were CM with foci of placental mesenchymal dysplasia (PMD). Two patients delivered live babies, and 2 patients with CM with twins developed lung metastasis.
Conclusion: Immunohistochemical analysis is a useful tool for the differential diagnosis of twin placenta with CM and morphologically similar conditions. In the present study, 2 cases were not twins with CM, but rather were diagnosed as CM with an androgenic/biparental chimera or

mosaic molar gestation and PMD. Immunohistochemical staining of the imprint gene products p57 and TSSC3 might be a useful screening tool for cytogenetic analyses.

PS-03-063

Differentially expressed microRNAs in cervical tumours, high-grade squamous intraepithelial lesions and benign lesions

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Objective: To explore the expression of several microRNAs (miRNAs) in cervical tumours, high-grade squamous intraepithelial lesions-HSILs (cervical intraepithelial lesions grade 3-CIN3) and benign lesions.
Method: RNA was extracted from a series of formalin-fixed paraffin-embedded cervical tissues: 48 invasive tumours, 46 HSILs and 20 benign lesions. The expression levels of miR-141-5p, miR-188-5p, miR-196-5p, and miR-877-3p were measured by quantitative RT-PCR. The expression of the ZNF177 gene, which was predicted in silico to be a target of miR-141 and miR-877, was also analyzed by immunohistochemistry (IHC).
Results: We found that the expression levels of all miRNAs but miR-141, was significantly higher in invasive tumours than in benign lesions ($p < 0.001$). Also, miR-188 and miR-196 expression was higher in HSIL than in benign lesions ($p < 0.001$). Concomitantly, ZNF177 expression was significantly lower in HSIL and invasive tumours than in benign lesions ($p < 0.001$). Furthermore, low nuclear ZNF177 protein expression was confirmed in invasive tumours by IHC. These results suggested that ZNF177 could be a target of these miRNAs, as predicted. No association was found between miRNAs or ZNF177 expression and overall survival, progression free- survival or other clinical variables.
Conclusion: HSILs and invasive cervical tumours display different miRNA expression pattern compared to benign cervical lesions.

PS-03-064

Correlation of microcystic, elongated and fragmented (MELF) pattern invasion with prognostic parameters in endometrial carcinoma

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Objective: To evaluate the presence of MELF pattern invasion in endometrioid endometrial carcinomas (EEC) and its association with the known prognostic parameters.
Method: 185 cases of EEC were reviewed to select tumours with and without MELF invasion. Double staining immunohistochemistry (D2-40/CD31) was performed to highlight lymphatic and blood vessels in the same slide. Tumour grade, stage, and frequency of lymphatic and blood vessels invasion were assessed in MELF negative and MELF positive tumours. The impact of MELF invasion on the overall survival of patients was estimated.
Results: MELF type invasion was present in 22 % cases. The majority of MELF positive tumours were grade 1 or grade 2 (93 %). MELF pattern invasion was observed mostly in FIGO stage IB (46 %). The frequency of lymphatic vessels invasion was significantly higher in MELF positive tumours than in MELF negative tumours (66 % vs 22 %, respectively). The frequency of blood vessels invasion was twice as common in MELF positive than in MELF negative tumours (22 % vs. 10 %, respectively). The presence of MELF invasion had no impact on overall survival.
Conclusion: MELF pattern invasion is associated with advanced myometrial invasion and LVSI, however, MELF pattern has no prognostic significance in EEC. We should consider the possibility that MELF pattern invasion is a side effect of advancing tumour invasion.

PS-03-065

Histopathological regress of serous ovarian carcinomas high-grade carrying BRCA germline mutation after neoadjuvant treatment

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Objective: Neoadjuvant platinum-based chemotherapy (NACT) is often used as a primary treatment for ovarian cancer (OC) in order to reduce tumour volume and make surgery more feasible.
Method: This study was aimed to compare histopathologic response to NACT in BRCA1-associated vs. sporadic high-grade serous OC. Scoring system suggested by Bohm et al. (see J. Clin Oncol., 2015, 33:2457–63) was used for evaluation of histopathologic response.
Results: Complete or near-complete histopathologic response (scores 2 and 3) was documented in 25/29 (86 %) BRCA1-driven vs. 65/122 (53 %) sporadic neoplasms ($p = 0.001$). In 63 cases (23 BRCA1/2-associated and 40 sporadic), data on platinum-free interval (PFI) were available. BRCA1/2-associated cases demonstrated longer PFI compared to sporadic OCs (6.9 vs 4.0 months, $p = 0.013$). Neither BRCA1/2-mutated nor sporadic OCs showed correlation between pathologic response and PFI duration. This lack of correlation may be explained by the selection of BRCA1/2-proficient cell clones during NACT, as demonstrated in pre-/post-NACT paired tumour samples obtained from BRCA1/2 mutation carriers.
Conclusion: BRCA1/2-driven OC demonstrate higher rate of complete or near-complete pathologic response. Limited prognostic value of pathologic response score is likely to be related to the selection of resistant OC cells during NACT. This work was supported by the Russian Scientific Fund (grant number 14-25-00111).

PS-03-066

Methylation study in the universal screening of Lynch Syndrome in endometrial and colorectal carcinoma

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Objective: One to three percent of endometrial and colorectal cancers (EC and CRC) show germline mutations in Miss Match Repair (MMR) genes, the hallmark of Lynch syndrome. A universal screening of the syndrome is advisable, including immunohistochemical evaluation (IHC) of MMR proteins and epigenetic and BRAF p.V600E mutation analysis. In the present work we analyze the incidence of MLH1 promoter hypermethylation in MLH1 IHC(-) EC cases and in MLH1 IHC(-)/BRAF p.V600E non-mutated CRC cases.
Method: A retrospective study of MLH1 IHC(-) CE ($n = 19$) and MLH1 IHC(-) and BRAF non-mutated RCC ($n = 9$) cases was performed. The degree of methylation of the MLH1 promoter was analyzed by bisulphite conversion analysis and subsequent pyrosequencing. Mutations of BRAF were determined by pyrosequencing.
Results: All of CE MLH1(-) cases (19/19) showed hypermethylation, all patients > 50 years. Three of the 9 CCR MLH1(-) non BRAF-mutated cases (33 %) exhibited MLH1 promoter hypermethylation.
Conclusion: a) The methylation study of MLH1 in EC MLH1(-) questions its indication in the universal screening algorithm of Lynch Syndrome in this neoplasia: MLH1 IHC(-) has been associated with an epigenetic origin, probably mainly in older patients. b) Given the significant percentage of MLH1 promoter hypermethylation in CCR non-mutated BRAF cases, the determination of this status, in MLH1(-) cases, is recommended.

PS-03-067

PD-L1 expression and overall survival in high grade endometrial carcinomas

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Objective: Endometrial carcinoma (EC) is the most frequent gynecological cancer in females. PD-L1 expresses in many cancer cells and has been shown to inhibit antigen-experienced T cells in the periphery, thereby protecting normal tissues from immune destruction. The purpose of the study was to assess the expression of PD-L1 in high grade EC and to correlate with overall survival (OS).
Method: We identify in a series of 740 patients diagnosed of EC, a high grade group. In this group we performed IHC staining for PD-L1, Estrogen and Progesterone Receptors, p53, p16, PTEN, β-catenin, HNF-1β, MLH1, MSH2, MSH6 and PMS2.
Results: We identified 177 high grade EC: 32 % grade III endometrioid carcinoma (ECIII) (n = 57) and 68 % non endometrioid tumours (NET). In ECIII was found MMR deficiency in 25 (44 %), PD-L1 tumour expression in 11 (20 %) and peritumoural expression in 36 (65 %). In NET was found MMR deficiency in 23 (22 %), PD-L1 tumour cell expression in 24 (22 %) and peritumoural expression in 65 (60 %). The OS in ECIII and NET were 87 and 52 months respectively. ECIII OS correlates negatively with MMR-intact, p16, p53 and PTEN. NET OS correlates negatively with age > 71, MMR-intact, PTEN and absence of PD-L1 peritumoural expression. Only MMR was an independent factor.
Conclusion: In both grade III endometrioid carcinoma and non endometrioid tumours, MMR deficiency is associated with better overall survival as independent factor. Peritumoural PD-L1 expression is associated with higher overall survival in non endometrioid tumours. We did not found prognostic significance in PD-L1 tumour cell expression.

PS-03-068

Molecular pattern of E-cadherin, CD44, COX2, and CD4 in squamous cell carcinoma of the uterine cervix with neoadjuvant therapy

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Objective: Although numerous studies demonstrated the efficiency of the neoadjuvant therapy (NAT) in different types of cervical carcinomas, the cellular parameters, which regulate the tumour response to this treatment, were not enough explored. We performed a comparative study of squamous cell carcinoma of the uterine cervix with and without NAT in order to demonstrate the utility of E-cadherin, CD44v6, COX-2, and CD4 in prediction of tumoural behavior.
Method: We analyzed the immunoexpression of E-cadherin, CD44v6, COX-2, and CD4 on formalin-fixed, paraffin-embedded specimens from 24 patients with cervical cancer, including 12 patients in stages IB-IIIB with first-line surgical treatment and 12 patients in stages IIB-IIIB, with NAT followed by radical hysterectomy.
Results: COX-2 immunostaining was significantly more intense in cases without or partial response to NAT as against the cases with a complete response. The CD44v6 immunoexpression was higher in more aggressive tumours, being involved in the response to NAT and E-cadherin immunoexpression was strong among the cases with NAT. CD4 had a higher immunoexpression in the cases with NAT.
Conclusion: The assessment of effectiveness of NAT in uterine cervix squamous cell carcinoma requires the discovery of new tumoural biological markers which will contribute to the implementation of new therapeutic strategies.

PS-03-069

Evaluation of the status of p53 in ovarian carcinoma: A comparative study of three methods of analysis

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Objective: By comparing the results of the immunohistochemical analysis with those obtained by genomic sequencing and the functional test, we tried to see if immunohistochemistry can be used as a first approach to select ovarian cancer cases that could justify mutation or functional alteration .
Method: This retrospective study was carried out at the Curie institute during the period between July 1989 and August 2004. 75 patients with epithelial-type ovarian cancer who underwent surgery were included. We noted: histological type, tumour grade, immunostaining with anti-P53 antibody, molecular biology.
Results: Overexpression of the P53 protein was demonstrated in 55 cases. Of the 56 mutated samples, 43 showed overexpression of p53 and among the 19 non-mutated, immunostaining was considered negative in 7 cases. The agreement between the results obtained by genomic DNA sequencing and those provided by immunohistochemical analysis of the protein was 67 %.
Conclusion: The comparison between the three techniques shows us that they are complementary. Sequencing is necessary to identify the type of mutation. The functional test is useful for defining the functional consequences of the molecular alterations observed by the sequencing. Immunohistochemical analysis is useful when there is no cryopreserved tissue for molecular analysis, and in the approach to early lesions.

PS-03-071

Metastatic pancreatic cancer to ovaries: An unusual case report of a mimicker of primary ovarian mucinous neoplasm

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Objective: Ovarian metastasis of pancreatic cancer is considered the prototypical example of a mimicker of primary ovarian mucinous neoplasm, accounting for nearly 14 % of all metastatic mucinous tumours in the ovary. We present the case of a bilateral ovarian tumour of a 56 y.o. woman with a history of non-operable pancreatic ductal adenocarcinoma under chemotherapy, diagnosed by FNA 5 months ago.
Method: Total hysterectomy was received, with bilateral nodular shape tumours of 18.5 × 13.5 × 10 cm and 13 × 10 × 10 cm in dimensions. Multiple sectioning showed grayish to yellowish and dark red lesions, solid and cystic areas with watery and mucinous material.
Results: The histological examination revealed cribriform and tubular formations consisted of pleomorphic cells with medium to marked atypia, mucinous cytoplasm, few goblet cells and central necroses. Borderline-like and cystadenomatous growth pattern as well as myxomatous and hemorrhagic changes were also observed. The immunohistochemistry revealed positivity for CK7, CEA, p53, p16, MUC-5AC, MUC-1, focal CA-125, isolated CK20 cells, loss of SMAD-4 expression, while MUC-2, CDX2, Pax8, WT1, PR and ER were negative. Proliferation index Ki67 was 30 %.
Conclusion: Although there was a significant histological similarity to primary ovarian mucinous carcinoma, patient's history, bilaterality and a pancreatobiliary immunophenotype confirmed the diagnosis of metastatic pancreatic ductal adenocarcinoma.

PS-03-072

Evaluation of Mismatch Repair (MMR) protein expression for Lynch syndrome screening in endometrial cancers in Turkish women: A preliminary study

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Objective: Women with Lynch syndrome(LS)are subject to increased risk of endometrial cancer(EC),along with colorectal cancer(CC). Our aim is to investigate the incidence of MMR protein expression in ECs.
Method: We applied MLH-1,MSH-2,MSH-6 and PMS-2 immunohistochemistry (IHC)in 155 endometrial tumours;chosen retrospectively between 2008 to 2016.IHC findings were compared with patient age, tumour grade, histologic type,pTNM and FIGO stages.
Results: Overall,%25,2 of cases exhibited loss of MMR proteins.28 cases showed MLH1&PMS2 loss(18.1 %), whereas 13 cases showed any loss other than MLH1 (7.1 %). MMR loss was most frequent in endometrioid carcinomas ($p = 0.046$). Grade III tumours showed the highest percentage (42.9 %) of non-MLH1 MMR loss ($p = 0.001$). 1 patient with MLH1&MSH2 loss had a history of CC, 1 with PMS2 loss had synchronous CC and 1 with MSH2&MSH6 loss had synchronous serous carcinoma in the ovary. Relation with other cancers were associated with non-MLH1 losses ($p = 0.019$).
Conclusion: Our study is the first data in Turkey; investigating MMR protein losses in ECs. Overall 25.2 % of cases showed MMR loss and most were associated with endometrioid morphology and higher tumour grade. Relation with other cancers revealed association with non-MLH1 losses. MLH1 methylation/mutation analysis of cases with MMR loss are yet to be performed. However our initial results highlighted a total 7.1 % loss in non-MLH1 proteins mostly associated with LS. This alone shows that a considerable number of patients need further evaluation; providing us a unique opportunity to save lives.

PS-03-073

Genetic characterisation of synchronous or metastatic endometrial and ovarian carcinomas by NGS

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Objective: Differentiation between simultaneous independent primary carcinomas, metastasis from the ovary to the endometrium or vice versa, is essential for prognostic and therapeutic considerations but may be very challenging because of shared morphological and molecular features.
Method: DNA from archived tissue from three patients with endometrioid ovarian and endometrial carcinoma (EOC/EEC) was analysed by sequence capture NGS with custom panel (219 kBp) on MiSeq (Illumina). Only non-synonymous variants with minimal coverage 100× and frequency 10 % were evaluated.
Results: In all cases (Case1: 29 years, EOC/EEC-G2; Case2: 45 years, EOC-G2/EEC-G3; Case3: 37 years, primary EOC-G1 + recurrent EOC/EEC-G1) tumours shared several likely germline or somatic mutations (BARD1,PIK3CA,PTEN; KIT,MET,MLH3,PIK3CA,POLE,POT1, PTEN,ZEB1; AKT1,ARID2,ATM,PIK3CA,POLE, for case1;2;3). Shared mutations suggest metastatic dissemination but we are not able to assess the primary site.
Conclusion: NGS analysis can be ancillary method in differentiation between synchronous tumours and metastatic disease, which is of clinical significance. In spite of clonal relation of tumours suggesting dissemination from one site to the other, other clinico-pathological parameters influencing tumours' behaviour should be considered as well, e.g. most patients with low grade and stage disease in both sites seems to have a favorable prognosis. However, other studies are needed. Supported by MZ CR conceptual development of research organisation 64165, General University Hospital in Prague.

PS-03-074

Reliability of intraoperative consultation in mucinous ovarian tumours

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Objective: Aim of this retrospective study is to assess the diagnostic accuracy of intraoperative consultation of ovarian mucinous tumours compared to final diagnosis and detect potential factors of misdiagnosis.
Method: A total of 105 specimens of mucinous tumours was evaluated using both frozen and paraffin sections. One or more sections were examined intraoperatively depending on tumour size and the degree of suspicion. Diagnostic parameters and their 95 % confidence intervals were also estimated.
Results: Out of 105 cases 45 were diagnosed as benign, 37 as borderline and 23 as malignant at the time of FS diagnosis, while 13 tumours had GI origin (12,4 %). The overall accuracy of the FS diagnosis accounted for 82,6 %. The median tumour size of overdiagnosed cases was 14,5 cm and underdiagnosed 24,5 cm. Sensitivity of FS is 95,1 , 79,4 and 70 % for benign, borderline and malignant tumours respectively.
Conclusion: Borderline and malignant mucinous ovarian tumours seem to be particularly prone to discrepancy between frozen and final diagnosis. Tumour heterogeneity, size and sampling errors consist the three most important factors of the decreased accuracy. Three or more sections from the most solid and complex foci should be performed in tumours larger than 22 cm. These limitations make difficult the intraoperative diagnosis of mucinous tumours.

PS-03-075

The role of omentectomy in staging of uterine serous carcinoma

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Objective: Uterine Serous Carcinoma (USC) comprises approximately 10 % of endometrial carcinomas, while it accounts for up to 39 % of endometrial cancer related deaths. Even when serous carcinomas are minimally invasive or confined to the endometrium, it seems that advanced-stage disease or recurrence is common. Recommendations for surgery in USC require full staging as in ovarian carcinoma and comprise total hysterectomy with bilateral salpingo-ophorectomy, omentectomy, abdominal washing for cytology and bilateral pelvic and para-aortic lymphadenectomy.
Method: A retrospective review of the records of patients with USC regarding surgical procedure, stage and histology results over a period of 12 years.
Results: A total of 144 women with USC were identified during the study period. Omentectomy was performed in 99 patients (68,75 %). Washing for cytology was positive in 25,69 % of patients. Omentum was involved in 28 patients (28,28 %). Six cases had gross negative and histologically positive omentum (21,43 %).
Conclusion: During surgical staging for USC visual and pathological omentum evaluation may differ and as a cause effect women with stage IV disease will be missed because of incomplete staging procedure. Despite the fact that the percentage of microscopic omental disease was low in our patients, we strongly believe that excision of normal looking omentum is necessary.

PS-03-076

Accuracy rate of intraoperative frozen section in the diagnosis of ovarian serous and mucinous neoplasms: About 99 cases

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Objective: This study was undertaken to evaluate the accuracy of intra-operative frozen section in the diagnosis of of ovarian serous and mucinous tumours.
Method: It was a retrospective study involving 99 cases of ovarian serous and mucinous tumours undergoing surgical resection with frozen section evaluation. The result of frozen section was compared with the final histopathologic diagnosis on paraffin sections.
Results: Out of 99 cases, 54 were diagnosed as serous tumour on final paraffin examination, while 45 were mucinous. The overall accuracy of frozen section diagnosis was 96.3 % for serous tumours and 71,1 % for mucinous tumours. Frozen section report had a sensitivity of 100 , 90,5 and 100 % for benign, malignant and borderline serous tumours. The corresponding specificities were 100 , 100 and 95.7 % respectively. The sensitivity of frozen section report was 100 ,33,5 and 65 for benign, malignant and borderline mucinous tumours. The corresponding specificities were 95.7 100 and 76 % respectively.The majority of cases of disagreement were in the mucinous and borderline tumours.
Conclusion: We conclude that frozen section has high accuracy rates for the diagnosis of benign and malignant ovarian serous tumours but the accuracy rates in borderline tumours remains relatively low especially for mucinous tumours.

PS-03-079

Primary bilateral ovarian lymphoma: Case report

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Objective: Primary ovarian lymphoma (POL) accounts for less than 1.5 % of ovarian neoplasms and less than 1 % of lymphomas present with ovarian involvement .The most common type is diffuse large B-cell lymphoma (DLBCL), followed by Burkitt lymphoma.
Method: We report a case of bilateral ovarian involvement by DLBCL with synchronous involvement of parts of the jejunum and its mesentery in a 38-year old patient. Macroscopically both ovaries were enlarged with white firm focally cystic cut surface.
Results: Microscopically diffusely infiltrating, medium to large, mildly pleomorphic lymphoid cells with oval-round nuclei and small nucleoli were observed. Numerous apoptotic bodies, necrosis and areas of sclerosis were present. Immunohistochemicaly the lymphoid cells were positive for CD20 and negative for bcl-2, CD5, CD23, CD30, Cyclin-D1, CD30, TdT. T-lymphocytes (CD3+) were also observed. Using Hans algorithm the cell of origin was classified as GCB-like (CD10 > 70 %, bcl6+, MUM1/IRF4 ~ 30 %). C-myc < 40 %. Proliferative index(Ki-67) ~ 98 %. No translocation of MYC, BCL-6 or BCL-2 was detected, using FISH technique. In situ hybridization EBER was negative.
Conclusion: Several criteria for accepting a case as POL have been proposed. An accepted definition of primary extra-nodal lymphoma, including ovarian, is that after routine staging procedures the extra-nodal localisation is the presenting site and constitutes the predominant disease location.

PS-03-080

Ovarian fibromas: A clinicopathological study of 18 cases

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Objective: The aim of the present study was to provide an updated overview on ovarian fibromas.
Method: We retrospectively reviewed eighteen cases of ovarian fibromas that were diagnosed at the pathology department of Mongi Slim hospital over a thirteen-year period (2002–2014).
Results: The patients of our series ranged in age between 18 and 75 years (mean = 42 years). The presenting clinical symptoms were dominated by pelvic pain (n = 11) and mass (n = 4), followed by metrorrhagia (n = 3), perimenopausal bleeding (n = 1) and menorrhagia (n = 1). All tumours were unilateral and the mean size was 8,77 cm. Twelve patients underwent unilateral salpingo-oophorectomy, whereas total hysterectomy and bilateral salpingo-oophorectomy was performed in five cases. Only one patient underwent tumourectomy. Histopathological examination of the surgical specimen confirmed the diagnosis of ovarian fibroma in all cases. All patients remained tumour free with no evidence of recurrence during a mean follow-up period of 17 months.
Conclusion: Clinical, ultasonographic and tumour marker data remain the best preoperative approach currently available for ovarian tumours. However, the diagnosis remains histological. Tumourectomy, if possible, is well indicated for young patients with ovarian fibromas; however, radical treatment is indicated for perimenopausal and menopausal patients.

PS-03-081

Metastatic carcinomas to the ovary: Clinico-pathological analysis of 13 cases

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Objective: The ovary is a common site of metastases and 5–30 % of ovarian masses are related to metastatic neoplasm. We aim to describe the clinico-pathological characteristics of ovarian metastasis.
Method: We reviewed records for 13cases ovarian metastasis with pathological consultation from 2008 to 2017 and retrieved clinical and pathological data.
Results: Metastatic ovarian malignancy has a prevalence of 27,66 %. The mean age of patients was 51,5 years (30–70). Primary malignancies were known in 4 cases and ovarian masses represent the first manifestation of the neoplasm in 9 cases. Bilateral involvement was found in 5 cases. On gross examination, mean size of the largest masses was 14,9 cm, it showed a multilocular and solid-cystic in 5 cases. Multiple small nodules on surface were observed in 3cases. Microscopically, all cases were classified as adenocarcinoma from which 54,5 % mucinous and 18,2 % signet ring cell. Vascular invasion was found in 3 cases. Direct pathological invasion was observed in 2 cases. In 8 cases, peritoneal dissemination was described. Primary malignancy were from the appendix (5cases), colon (5cases), stomach (2cases) and endometrium (1case).
Conclusion: Secondary tumours of the ovary are rare and it can be challenging to distinguish a primary ovarian malignancy from metastases so multiple diagnostic approaches are necessary.

PS-03-084

Pleomorphic sarcoma and squamous cell carcinoma (SCC) in an ovarian cystic teratoma: A case report of an extremely rare malignant transformation

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Objective: Malignant transformation in a mature cystic teratoma (MCT) is rare(less than 2 %),most frequently is squamous cell carcinoma(SCC). Sarcomatous change is even rarer with limited reported cases till date

Method: We report a case of pleomorphic sarcoma(PS) and SCC arising in an ovarian MCT in a 41 year-old female.Pelvic CT and U/S revealed an 20 × 18 cm cystic-solid ovary mass.A total hysterectomy,bilateral salpigo-oophorectomy and partial omentectomy were performed.

Results: Grossly the tumour was encapsulated with a smooth surface. About 35 % was occupied by a cyst contained sebaceous material and hairs. The remaining(65 %) was solid with a gray-white firm consistency. Microscopically the cyst revealed a MCT. Cyst's-wall was delimited by squamous epithelium with transitional areas from dysplastic to "IN-SITU" and superficially infiltrating SCC. The solid component showed a pleomorphic, epitelioid and spindle-cell sarcoma with bizarre neoplastic giant cells, hight,atypical mitotic activity(30/10HPF), necrosis and a chronic inflammatory infiltrate with osteoclast-like and Touton giant cells. Immunohistochemically the squamous component stained positively for EMA,P63,CK5/6 and the sarcomatous only for Vimentin. Ki67 ≥ 80 %. Pankeratin, EMA, SMA, Caldesmon, S100p, CD34, HMB45, ER, PR,were negative. According these findings a diagnosis of a pleomorphic sarcoma and SCC arising in an ovarian MCT was rendered.

Conclusion: Malignant transformation of an ovarian MCT showing both sarcomatous and carcinomatous elements, as in our case, is extremely rare. A preoperative accurate diagnosis is difficult. Definite diagnosis is achieved by careful and thorough histological evaluation.

PS-03-085

Expression of CD133 and CD44 in serous ovarian cancer and peritoneal metastasis

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Objective: The CD133 and CD44 are the most commonly used markers for putative cancer steam cells (CSCs), especially for ovarian CSCs, but its clinical significance remains uncertain. The aim of this study was to compare the expression of CD133 and CD44 and to examine their potential clinical role.

Method: We analyzed immunohistochemically assessed expression of CD133 and CD44 in 69 cases of primary ovarian carcinoma and their peritoneal metastasis. Staining data were correlated with clinicopathological characteristics and patient outcome.

Results: CD133 expression was mainly seen in the apical/endoluminal surface of tumour cells and was found in 58 % of carcinoma and 42 % of metastasis. CD44 expression appeared mostly as a membranous stain and was found in 29 % of carcinoma and 46 % of metastasis. Multivariate analysis showed the difference in time to progression and time to survival for CD133 expression in tumour ($p = 0.004$ and 0.016, respectively), and the difference in time to progression and time to survival for CD44 expression was not found. Cox's proportional hazards model identified expression of CD133 protein in tumour as independent prognostic factor.

Conclusion: Our study indicate that the immunohistochemical assesment of CD133 expression may have potential clinical value in predicting disease progresssion or prognosis in serous ovarian cancer patients.

PS-03-086

High grade serous ovarian carcinoma in a patient with BRCA2 mutation, clinicopatholocigal study, treatment and evolution

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Objective: Highlight the importance of comprehensive study of patients (clinical diagnosis, pathological diagnosis, genetic study and treatment) to achieve a good result.

Method: A 61-year-old woman. Background: Sister died at age 50 due to breast cancer. She presented hypogastric pain, increased abdominal perimeter and intestinal occlusion. CA125: 1405 U/ml. CT: Mixed right adnexal mass, peritoneal implants and ascites. She was treated with 4 cycles of neoadjuvant chemotherapy and surgery: bilateral anexectomy, omentectomy, appendectomy and resection of small intestine implants.

Results: Solid-cystic ovarian tumour, 1.3 × 1 cm, papillary histological pattern, pleomorphic cells, frequent mitosis, vascular permeation and psamoma bodies. Immunohistochemistry: Estrogens (2+), Progesterone and Calretinin (-). Ki67: 10–20 %. The Fallopian tube, omentum, appendix and small intestine presented tumour infiltration. FIGO stage: IIIC. Patient completed chemotherapy (6 cycles: Carboplatin + Paclitaxel) and was derived to the Genetic Counseling Unit detecting a mutation in BRCA2 gene. One year later, she presented peritoneal recurrence, treated with chemotherapy (6 cycles: Pegylated liposomal doxorubicin + Trabectedin). Currently asymptomatic and in remission.

Conclusion: Serous ovarian tumours positive BRCA are infrequent (15 %) and aggressive (5 year survival stage IIIC 39 %), so the evolution of this case is interesting. A good diagnosis is the basis for treatment; also genetics is important because of heredity and prevention.

PS-03-088

Histopathologic features of advanced stage endometrial carcinoma

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Objective: The aim of this study is to document the histopathologic features of endometrial cancer(EC) cases with tubal involvement.

Method: Twenty-nine advanced stage EC cases were included in the study. There were 18 cases with fallopian tube involvement. Four cases were associated with positive peritoneal cytology.

Results: There were three cases that are under 60 years old with superficial myometrial invasion and these cases were associated with endometriosis. In all those cases that are above 60-year-old there were deep myometrial invasions and 6 cases had cervical involvement. There was a significant inverse correlation between cervical involvement and endometriosis in the EC cases ($P < 0.05$). Endometriosis was associated with the cases under 60 years old ($P < 0.05$). The patients having immunohistochemical features of T cell factor/APC/β-cathenin pathway were mostly under 60 years old ($P < 0.05$). Among these group three patients had additional abnormalities, which are dual loss of MLH1 and PMS2, and strong p53 positivity. In cases above 60 years old, PTEN inactivation, loss of PAX-8 and aging were detected.

Conclusion: Fallopian tube sampling according to SEE-FIM protocol is necessary for true histopathologic classification of EC cases.

PS-03-089

A rare case of a common benign tumour: Bilateral lipomas of the fallopian tubes

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Objective: Although lipoma is a common tumour for many anatomical sites, tubal localisation is rare and bilateral existance is exceptional. Here, we would like to present our case; a 49 years old woman operated for adenomyosis.
Method: Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Postoperative recovery was uneventful and the patient was discharged from hospital on the second day of the operation.
Results: The uterus measured 12 × 8 × 6 cm. Bilateral salpingo oophorectomy specimen were sent seperately; and two encapsulated, soft, yellow nodular mass measuring 2 cm were located on both fimbrial sides of the fallopian tubes with a smooth and intact outer surface. On microscopic examination, the two lesions were entirely composed of mature adipocytes. There was no evidence of malignancy.
Conclusion: Although CT scans gives important clues to guiding a differential diagnosis for adipose tumours, bilateral mass lesions on tuba uterina raises the doubt for a metastatic disease radiologically. We would like to share this rare entity with the participants of the Europian Congress of Pathology.

PS-03-092

Combined large-cell neuroendocrine carcinoma and endometrioid adenocarcinoma of the endometrium: A case report

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Objective: Large cell neuroendocrine carcinoma (LCNEC) of the endometrium is a relatively rare and usually aggressive malignancy. We report a case of an endometrial tumour that was a combination of a LCNEC and endometrioid adenocarcinoma.
Method: A 58-year-old woman presented with postmenopausal vaginal bleeding. Explorative curettage revealed a LCNEC of the endometrium. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and was diagnosed as having FIGO stage IB endometrial carcinoma. In spite of refusal of adjuvant therapy, and irregular follow-up, she has been well with no evidence of disease for 52 months following surgery.
Results: Grossly, a polypoid neoplasm measuring 6.5 × 2.2 × 2.5 cm, infiltrating more than a half of the thickness of the myometrium of the posterior uterine wall was found. Histologically, the tumour was composed of two components: a predominant large cell high-grade neuroendocrine carcinoma and a minor superficial well-differentiated endometroid adenocarcinoma with foci of squamous differentiation. There was a differential immunoreactivity between the two components. More than 10 % of the cells of the LCNEC were positive for three neuroendocrine markers (CD56, NSE and synaptophysin), showing also diffuse positivity for cytokeratin 18, vimentin, and p16, and hormone receptor negativity, whereas the majority of the cells of endometroid carcinoma were negative for neuroendocrine markers, hormone receptor positive and only focally p16 positive. The proliferative index determined by Ki-67 was higher in LCNEC in which p53 overexpression was also present.
Conclusion: Immunohistochemical analysis is helpful in diagnosing and differentiating primary LCNEC. The presented case also confirms that early stage polypoid LCNEC may have a more favourable prognosis.

PS-03-093

Pigmented vulvar basal-cell carcinoma: Report of two cases and review of the literature

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Objective: Basal cell carcinoma (BCC) is the most common non-melanocytic skin cancer, typically arising in sun-exposed area.It may arise on non-sun-exposed sites, including the vulva, where accounts for less than 5 % of all neoplasms. We report the cases of basal cell carcinoma of two women, aged 79 and 66, that showed a pigmeted bleeding vulvar lesion with ulcer.
Method: After the diagnosis of BCC (punch) both patients had wide excisional biopsy;
Results: Pathological data were similar to skin pigmented BCC. The margins were free. None of them developed local recurrence y/o distant metastasis
Conclusion: Basal cell carcinoma of the vulva is rare and an accurate diagnosis depends upon a high index of suspicion, biopsy and histopathologic examination. Treatment of choice consists of surgical excision with tumour-free margins Complete local excision is curative, although the recurrence rate is high, and metastases have been reported. Long term follow-up is necessary.

PS-03-095

Endometrial receptivity in patients with Uterine Myoma (UM) after previously performed ineffective Uterine Artery Embolisation (UAE), Focused Ultrasound Ablation (FUA) and Myomectomy (ME)

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Objective: The aim of the study was to endometrial receptivity in reproductive-age women suffering from UM after ineffective UAE, FUA and ME.
Method: The study was made on pipelle-biopsies of endometrium taken from 39 reproductive-age women (36,2 ± 5,2 years) suffering from UM after ineffective UAE (13), FUA (13) and ME (13) in secretory phase after ineffective treatment (group A) and 3 months later after repeated ME (group B). Histological and immunohistochemical (IHC) examination was performed with primary antibodies to PgR, ER and LIF.
Results: Morphological analysis of endometrium showed retarding endometrial maturation, decrease in pinopodes level, decrease in PgR, ER and LIF in group A, these characteristics were improved in group B. The worst ER and PgR and the lowest LIF were in patients after FUA, a little better in patients after UAE. In patients with ME stromal PgR/ER index was the best in groups A (1,91) and B (1,98) and LIF expression was higher (1,9 and 3,8, respectively).
Conclusion: Obtained results show better endometrial receptivity after inefficient ME, compared to UAE an FUA, with the worst parameters in the latter group. Nevertheless, all patients show improve of endometrial implantation potential in 3 months after repeated myomectomy supporting the idea of reversibility of these changes.

PS-03-096

Expression analysis of tollip, the inhibitor of inflammatory signaling cascade, in placenta samples in cases of early onset preeclampsia

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Objective: The aim was to study the inhibitor expression of inflammatory signaling cascade, Tollip, in placenta samples in cases of early- (EPE) and late—onset (LPE) preeclampsia.
Method: The immunohistological study was performed on the 20 paraffin-embedded slices of placenta using Tollip primary monoclonal antibodies (1:200; Termo scientific). Groups with PE included 5 women with EPE and 5—with LPE. Control groups included 5 women with normal pregnancy (late control–LP), 38–39 gestation weeks, 5 samples—26–30 weeks (early control–EC). The intensity of immunohistochemical reaction was estimated by means of Nikon Eclipse microscope imaging software (NIS-Elements).
Results: The immunohistochemical study in control groups indicated Tollip cytoplasmic staining in placenta: amnion cells, major&minor subset of decidual cells, syncytiotrophoblast, syncytial knots, mesenchymal stroma cells, endothelium of blood vessels of villi. Tollip demonstrated less intensive expression in decidual cells in women with EPE than EC (0,059+ 0,0081 and 0,067+ 0,0041, respectively; $p < 0,05$). Expression in endothelium of intermediate placental villi was lower in EPE (0,037 + 0,092), than in EC (0,047 + 0,062) ($p = 0,08$). In cases of LPE expression Tollip in placenta samples was not shown significant differences.
Conclusion: Decreased expression pro-inflammatory activity blocker Tollip in EPE demonstrates an important role in the genesis of EPE.

PS-03-097
The disturbance of opportunistic placenta microflora as a trigger for preeclampsia pathogenesis
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Objective: The aim of the study was to analyze histological and microbial features of placenta in cases of preeclampsia (PE).
Method: The group with PE included 20 women with PE and 12 women with physiological pregnancy (Control group), of reproductive age, 26–39 gestation weeks after cesarean section. We performed histological (hem&eosin staining) and microbiological examinations.
Results: By histologic study we revealed chronic villitis of unknown etiology (VUE) (reflecting interruption of the tolerance of the mother's organism in relation to the fetus) in 45 % cases of PE ($p < 0.05$) (with predominantly multi-focal and patchy lesions of the villous tree). In the control group chronic villitis was observed in 8.3 % and it was revealed only focal lesion Moreover, some isolates were observed by microbiological examination of placenta in 25 % cases: Streptococcus agalactiae, Steptococcus oralis, Propionibacterium acnes, Actinomyces oris, Staphylococcus warneri. There was no growth of microorganisms in the control group. Disturbances of the placenta microflora were proposed to associate with chronic villitis.
Conclusion: Thus, opportunistic microorganisms may be triggers of inflammatory cascade activation and resulting to preeclampsia. Notably, microorganisms were revealed in late-onset preeclampsia (after 34 weeks gestations, is considered to associate to mother's pathology) only.

PS-03-098
Adenomatoid tumours of uterus: A case report
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Objective: Uterine adenomatoid tumours are rare, benign neoplasm originating of serosal mesothelium. They typically occur in women of reproductive age, are usually asymptomatic and usually identified as leiomyomas in gross appearance.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 35 year-old-women underwent a hysterectomy for paraovarian cyst and leiomyoma. Grossly, a solitary, well-circumscribed, subserosal mass, measuring 7 cm in greatest dimension identified in the uterine corpus. It had a white, whorled apperance on cut section. Histologically, subserosal lesion was nodular proliferation of variably sized tubules and cysts lined by eosinophilic cuboidal or flattened cells. The cells lining the gland –like structures had small-to-moderate amounts of pale, often vacuolated cytoplasm and small. Nuclear pleomorphism and mitotic figures were not seen. The epitheloid cells stained strongly for calretinin, pancytokeratin, vimentin, focally for WT-1 and were negative for CD34,SMA, CD10.
Conclusion: Adenomatoid tumours are characterized by adenoid, angiomatoid, solid and cystic pattern. The most cystic examples can simulate lymphangioma.The mesothelial cell origin has been established on the basis of an immunohistochemistry stain using calretinin. We would like to report a rare case of adenomatoid tumour, which is a rare benign histologic process.

PS-03-099
Paediatric ovarian masses in South Tunisia: A clinicopathological study of 40 cases
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Objective: We propose to analyze the epidemiological and pathological characteristics of the ovarian masses in children.
Method: Forty cases of ovarian masses occurring in girls under 16 years old were collected by the Pathology Department of Habib Bourguiba Hospital over an 11-year period (2006–2016); an analysis of the histological data and a review of the clinical records were carried out in all cases.
Results: The average age of our patients was 13.9 years. Non-neoplastic lesions accounted for 75 % of cases (average age = 14.3 years). Follicular cysts were the most frequent non-neoplastic lesions (80 %) followed by serous cysts (13.3 %) and the ovarian torsion with infarction (6.7 %). The ovarian tumours accounted for 25 % of cases (average age = 14.2 years). Germ Cell Tumours were the most frequent neoplastic lesions (80 %), (average age = 13.7 years). These tumours were mostly benign (75 %: mature cystic teratoma) and malignant in 2 cases. Benign serous tumours were more rare (20 %).
Conclusion: Ovarian tumours are rare in childhood. In our study, they represent ¼ of the ovarian masses. We noted that they are mostly benign, which was similar to published data, and dominated by Germ Cell tumours, especially mature cystic teratomas.

PS-03-100
Extrauterine pregnancies: Presentation of cervical and pelvic pregnancy
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Objective: Extrauterine pregnancies represent nearly 1 % of all pregnancies. Although mortality decreased to 4 % thanks to the diagnostic methods used nowadays, ectopic pregnancies are the first cause of maternal mortality during the first trimester of pregnancy.
Method: We report the first case of a 30 years-old-woman who presented with acute abdominal pain and ultrasound findings were consistent to an ovarian tumour. She had an emergency surgery and the histological examination of the tissue we received, 7 cm in greatest diameter, showed chorionic villi, blood and fibrin.
Results: The second case was a 27-years-old woman at the first trimester of pregnancy, who underwent endometrial curettage because of vaginal

bleeding and no development of the embryo. The bioptic tissue consisted mostly of chorionic villi and a small piece of endocervical tissue with syncytiotrophoblastic elements.
Conclusion: Abdominal ectopic pregnancies may simulate pelvic tumour-like lesions and one must always keep in mind of this possibility in a fertile woman, so exact diagnosis be made. Moreover, in case of a cervical pregnancy the miscarriage may lead in accessing bleeding and life threat situation. Women who had an ectopic pregnancy in the past are more prone to have another one in the future.

PS-03-102
Brenner tumour in a young, pregnant woman
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Objective: Brenner tumour is a rare ovarian tumour, mostly found in elderly ladies (aged 50–70 years). These neoplasms morphologically are classified as benign, borderline and malignant. The benign subtype is the most frequent but it accounts for only 5 % of benign ovarian neoplasms (WHO, 2015).
Method: Patient's medical history, clinical and laboratory findings, as well as the treatment and surgical pathology data were retrospectively reviewed.
Results: A 23-year-old woman, G2P0 was admitted to hospital because of pathological pattern in cardiotocography. For child's benefit, the patient underwent Caesarean section disclosing also polycystic right ovary that was removed. At gross pathologic evaluation, a polycystic, firm, greyish brown mass, measuring 4.5 × 2.5 × 2 cm, was found. Histologically, sharply demarcated epithelial nests in a fibrous stroma were detected. Epithelial cells mostly were cylindrical, followed by cuboid or transitional architecture. Cysts were found in some nests. The morphological picture was consistent with a benign Brenner tumour. Postoperative recovery was uneventful, and patient together with healthy newborn girl was discharged from hospital 4 days after surgery.
Conclusion: 1) Brenner tumour can occur in young pregnant women. 2) The differential diagnosis of cystic ovarian masses in pregnancy should include Brenner tumour as well.

PS-03-103
Primary vaginal mucinous adenocarcinoma: A case report and review of the literature
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Objective: Primary mucinous vaginal adenocarcinoma is an extremely rare entity with uncertain histogenesis. We report a case and describe the histopahological features of this unsual tumour
Method: We report the case of a primary mucinous adenocarcinoma of intestinal type in a young woman with a poypoid lesion in the posterior wall of vagina.
Results: A polypoid lesion was excised with margins. Microscopic examination revealed a proliferation of glands with complex arquitecture lined by stratified columnar cells with little intracitoplasmic and extracellular mucin stained wirh Alcian Blue/ periodic acid- Schiff
Conclusion: Primary mucinous vaginal adenocarcinoma comprises only 1–2 % of all gynecologic malignancies. Most frequently vaginal adenocarcinomas are metastatic.Recognition of this rare entity is important, particularly to avoid the misdiagnosis of secondary tumour.

PS-03-104
Copeptin and sodium plasma levels in preeclampsia
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Objective: Copeptin is a glycopeptide, part of the pre-hormone molecule of the antidiuretic hormone. Copeptin takes a part in sodium level regulation and considered to be one of the biomarkers of cardiovascular diseases. The aim of study was to evaluate maternal plasma concentrations of copeptin and sodium in preeclampsia (PE).
Method: 30 health women with normal pregnancy (Control) and 29 with pregnancy complicated with PE of reproductive age, 32–39 gestation weeks. Copeptin level in blood plasma was estimated by enzyme-linked immunosorbent assay (Cloud-Clone-Corp., USA). Measurements of sodium level were made in Medica electrolyte analyzers (Medica, USA).
Results: Our study showed that Copeptin level in plasma was higher in PE group (397,4 ± 52,31 pg/ml) than in Control (276,3 ± 58,58 pg/ml) ($p < 0,05$). The sodium plasma concentration in PE was lower than normal pregnancy group (129,6 + 0.341 mmol/l vs 137 + 0.42 mmol/l, ($p < 0,05$).
Conclusion: We revealed significant differences in blood plasma balance of ions and Copeptin level in normal pregnancy and preeclampsia. Increased Copeptin level was associated with significant reduction of sodium plasma level in PE. Dysregulation of Copeptin-sodium balance is one of the key in PE pathogenesis.

PS-03-105
Endometrial clear cell carcinoma of a postmenopausal woman: A case report
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Objective: Endometrial cancer is the most common gynecologic malignancy in developed-countries. Clear cell carcinoma(CCC) typically occurs in the ovaries and is rarely seen in the cervix and the endometrium.
Method: A 54-year-old woman was admitted to our Gynecology&Obstetrics clinic with postmenauposal vaginal-bleeding. She only used to have medical therapy for hypertension and diabetes. The serum level of Cancer-antigen-125(CA-125) was 48.7 U/mL and ultrasonography demonstrated a 2.5 cm mass in endometrial-cavity.
Results: The histopathologic evaluation of curettage-material indicated a malignant tumour composed of clear cells. Positron-emission-tomography/computed-tomography(PET/CT) showed only hypermetabolic lesions in the endometrial-cavity and pelvic-lymph-nodes. Total abdominal-hysterectomy with bilateral salpingo-oophorectomy(BSO), pelvic and paraaortic lymph-node dissections, omentectomy were performed. Microscopically the tumour in endometrium was purely composed of clear cells that were positive- stained with Estrogen-receptor(ER),Vimentin and negative-stained with p16, Carcinoembriyonic-antigene, Human-Papilloma-virus, Renal-cell-carcinoma-antigene(RCC). The tumour was diagnosed as CCC of the endometrium. The depth of the tumour was less than half-thickness of the myometrium. 3 metastatic lymph-nodes were present in both pelvic lymph-node dissections. Postoperative chemotherapy and radiotherapy were performed and the patient is currently under follow-up for one-year without any recurrence or metastasis.
Conclusion: CCC representing about 3 % of all endometrial carcinomas(ECs) is suggested to have a relatively-poor prognosis and characterized by late-recurrence compared to other ECs.

Sunday, 3 September 2017, 09:30–10:30, Hall 3
PS-04 Infectious Diseases Pathology

PS-04-002
Actinomycosis as an aetiologic agent of refractory tonsillitis: A case report and review of literature
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Objective: To describe a case of refractory tonsillitis in an adult, sequel to granulomatous inflammation induced by Actinomycetes. To perform a review of relevant literature on the relationship between Actinomycosis, refractory tonsillitis and tonsillomegaly.
Method: Preparation of 3–4 micron thick sections tonsillectomy biopsy obtained from a 51 years old female with refractory tonsillitis. Histologic analysis of morphologic features in sections stained with Hematoxylin and Eosin.
Results: On histology, a fibro-inflammatory process characterized by effacement of lymphoid tissue and neighbouring salivary gland acini is observed. Focal areas of necrosis and a patchy mixed inflammatory infiltrate are observed. Multiple clusters of radially arranged filamentous basophilic organisms were seen within the tonsils. A marked necro-inflammatory reaction is observed adjacent to these clusters. A diagnosis of Actinomycosis was made, prompting definitive treatment with antibiotics.
Conclusion: Refractory tonsillar hyperplasia in adults, in contrast to children is indicative of relatively sinister aetiologies. Actinomycosis is a documented cause of tonsillomegaly in adults. It is a rare disease, and misdiagnosis is common. Microscopy is the gold standard for definitive diagnosis and as such histologic examination is essential for all tonsillectomy specimens.

PS-04-003
Case report and review literature of parasite testicular mass mimic to tumour
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Objective: Parasite infestation of the testis by parasite is rarely reported and may present with few clinical signs, depending upon the stage. It may mimic a testicular tumour and we have to differentiate it. We present a case of a 51-year-old man who presented with testicular swelling and discomfort for 6 months.
Method: Clinical examination, ultrasound and imaging suggested an intrascrotal cystic lesion with a normal testis. However, the intraoperative findings revealed a tumour-like mass; hence, a orchidectomy was performed.
Results: Histopathology reported a diagnosis of a cystic testicular tunica and spermatic cord with parasite infection by filaria. Cyst was found, 6 mm in diameter, the wall of which was formed by a fibrous tissue with thin-walled capillaries. There are infiltration of histiocytes, eosinophils, lymphocytes with single giant multinucleated cells of foreign bodies. In the cyst cavity, the body of a filaria was found.
Conclusion: Here, we review the literature of scrotal and testicular parasite disease and discuss the course of the appropriate diagnostic management and differential diagnosis involved.

PS-04-004
Pathogens associated with female genital tract infections in Kabul
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Objective: To determine the vaginal pathogens associated with Genital Tract Infections
Method: A cross sectional study design, over a 24-month period between July 2012 to June 2014, at the Department of Microbiology, Clinical Laboratory of French Medical Institute for Mothers and Children, microbiological analyses on samples were carried out vaginal and high vaginal swab samples were obtained from women of reproductive age with suspected genital tract infections and percentage frequencies of isolates were determined comparatively. Samples were screened for the presence of vaginal pathogens using conventional microbiological techniques. Chocolate agar was used for the isolation of fastidious organisms, Chromagar Candida was employed to isolate and enumerate Candida species, Bromocresol Purple agar was used for isolation of members of Enterobacteriaceae while Blood agar base in 10 % CO2-enriched atmosphere was employed for the isolation of Gardnerella vaginalis. Microscopic examinations of smears were carried out to determine the presence of pus cells, yeast cells or 'clue cells'
Results: Out of 1297 samples, 550 (42.4 %) yielded the growth of a pathogen. Gardnerella vaginalis recorded the highest prevalence of 184 (33.45 %), followed by Candida species 135 (24.55 %), members of Enterobacteriaceae altogether 130 (23.64 %), Gram-positive cocci 92 (16.73 %) while Neisseria gonorrhea recorded the least prevalence of 03 (0.55 %). Among the Candida isolates obtained, Candida albicans was more frequently isolated as compared to non-albicans Candida
Conclusion: Vaginal pathogens are directly associated with genital tract infections and this is on the highly prevalent among women in the developing countries like Afghanistan. There is a dire need for routine evaluation and appropriate intervention in antenatal clinics

PS-04-005
Infectious diseases - my best lung transplant case
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Objective: Infection of the pulmonary allograft after lung transplantation is known to have a negative impact on outcome. Pathological diagnosis can be challenging, as differential diagnosis includes antibody-mediated or cellular rejection, which share similar histopathological features.
Method: We report a case of a 60-year old patient who underwent double lung transplantation for sarcoidosis. Postoperative period was uncomplicated. The patients represented with symptoms of infection 6 month after lung transplantation.
Results: Transbronchial biopsies of the pulmonary allograft were negative for acute cellular rejection and there were no morphological features of antibody-mediated rejection but organizing pneumonia pattern. Bacterioscopic stains were negative for microorganisms. Focal squamous cell metaplasia was present in intrapulmonary airways. Corresponding autolytic BAL-material contained besides respiratory cells many multinucleate macrophages and showed neutrophil granulocytosis. Immunohistochemistry was negative for Herpes simplex types 1 &2 but few budding yeast, compatible with Candida spp were present.
Conclusion: BAL represents an important diagnostic tool and complements transbronchial biopsies in the diagnostic setting of infectious diseases in pulmonary allografts.

PS-04-006

Extrapulmonary tuberculosis: About a series in Algeria

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Objective: To list the most frequent extrapulmonary localisations of tuberculosis and to identify unusual locations. Extrapulmonary tuberculosis (EPT) is in constant augmentation (20 to 40 % according to different series) in developed and developing countries and the World Health Organization reports 14 % of EPT without concomitant pulmonary infection.
Method: 90 cases of EPT are collected during last year in the Unit Pathology of Mustapha Pacha Universitary Hospital coming from several surgical departments : orthopaedic,visceral, head and neck, gynaecological. All specimens are embedded in paraffin and stained with hematoxyline-eosine.Morphological exam is performed with optical microscope.
Results: Tuberculosis is found in about one third in lymph nodes particularly those cervical , near one third is located in pleura, the other cases concern peritoneal tissue, intestinal tract, skin, liver, cavum, bone, salivary gland, testis, female genital tract,synovial membrane and an uncommon location in an angiomatous polyp of nasal cavity.
Conclusion: In Algeria EPT reaches 61, 9 % in 2014 according to the Algerian Public Health Ministry, a higher rate than those seen in other parts of the world probably in relation with pastoral regions and with migratory flows in south Sahara. EPT is often misdiagnosed by clinicians and physicians because of these inusual locations, by pathologists due to a lack of caseous necrosis in some of these lesions and by microbiologists because of very low amounts of Kock's bacillus.

PS-04-007

Histopathological changes due to influenza viruses

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Objective: There are only few publications considering histopathology directly related to influenza virus.
Method: 85 autopsy cases in adults were studied during period 2009–2017. Diagnostics included RT PCR and IHC of lungs with serum against influenza A virus. Histopathology was compared with observations during previous epidemics. We distinguished changes due to influenza virus and other pathogens.
Results: Most common appeared to be cytopathic effect on the cells of respiratory tract epithelium, alveolocytes and macrophages with enlargement of slightly basophilic cell cytoplasm and later cytolysis with general duration about a week. During the epidemic due to A/California/04/2009 H1N1 in 2009, 2011 and 2016 nearby the signs of RDS we observed also cytoproliferative changes of infected cells leading to formation of multinucleated giant cells and metaplasia, corresponding with clinical peculiarities of the disease with general duration about a month. Cases despite the negative result of PCR were considered as influenza basing upon histopathology and results of IHC, which demonstrated virus antigens in endothelial cells of different organs, neurons, and in alveolar macrophages even in cases with pneumonia but without clinical and pathological signs of typical influenza.
Conclusion: Influenza causes typical cytopathological changes related to strain properties. The phenomenon of chronic/latent lesions has to be studied further.

PS-04-008

Pseudo-tumoural presentation of bladder bilharziasis

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Objective: Urinary Bilharziasis is an endemic parasite in Africa, totally eradicated in Tunisia. In recent years, this pathology has become a rare pathology, and is less known to the clinician and pathologists. Its presentation as a bladder tumour has rarely been reported.
Method: We report two cases of a rare form of presentation of Bilharzia and discuss its anatomo-clinical characteristics.
Results: The first patient was a 78-year-old man, hospitalized for dysuria. Cystoscopy showed a pedicled bladder tumour. Pathologic examination concluded that low-grade papillary urothelial carcinoma. He was put on therapy with good initial response. After 3 years of follow-up, cystoscopy revealed the presence of several tumours taking up all the bladder walls. Histological examination showed diffuse inflammatory lesions in the bladder and prostate with several Bilharzie eggs without any tumour residue. The second patient was a 44-year-old woman who consulted for terminal hematuria. Cystoscopy showed a reddish congestive and tumour. Endoscopic resection was performed. The histological examination concluded of a chronic cystitis related to bilharziasis.
Conclusion: These observations highlight the diversity of clinical, radiological and pathological aspects of urogenital bilharziasis in non-endemic areas and the necessity in some cases to refer to this diagnosis in the presence of hematuria.

PS-04-009

A "Linear Lichen Planus" in travelers may be a harbinger of schistosomiasis

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Objective: Bladder biopsy is diagnostic for Schistosoma hematobium infection but characteristic skin symptomatology may be also helpful. The aim of this case report is to illustrate practical difficulties in diagnosing urinary schistosomiasis in non-endemic areas.
Method: A 17 year-old female immigrant from Senegal (West Africa) presented with linear and raised skin lesions on lower extremities of 2 months duration. After the biopsy diagnosis of lichen planus was treated with topical steroids. The lesions were waxing and waning. After 3 years, because of self-reported hematuria, dysuria, suprapubic pain, bacteriuria, proteinuria and negative cultures, she underwent bladder biopsy.
Results: The histology of skin lesions was consistent with lichen planus because of compact orthokeratosis, hypergranulosis with mild acanthosis, elongation of papillae, basal vacuolization, lichenoid chronic inflammation and pigment incontinence. The histology of three papillary lesions found near the dome of the bladder on cystoscopy 3 years later showed severe cystitis with eosinophilia, dystrophic calcifications, and numerous Schistosoma hematobium eggs.
Conclusion: In non-endemic areas, if the health care providers are not aware of the travel status or country of origin of the patient, and in absence of urinary symptoms, even if the typical lichen planus-like lesions are present, the diagnosis of schistosomiasis may be delayed.

PS-04-010

Immediate death causes in influenza

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Objective: Influenza remains a widespread disease leading to lethal outcomes. Immediate death causes are seldom analyzed.
Method: 90 autopsy cases in adults were studied during period 2009–2017. Diagnosis was based upon RT PCR. Histopathology was compared with observations during previous epidemics.
Results: Following variants of immediate death causes are evaluated: 1) acute respiratory insufficiency due to respiratory distress syndrome (more

typical for A/California/04/2009 H1N1 in 2009, 2011 and 2016); 2) generalized infection, usually with brain involvement (more typical for children in 70–80th of XX century); 3) local complications—bacterial (including chlamydia), mycoplasma and fungal pneumonia (more typical for adults in 70–80th of XX century and 2017); 4)deterioration of chronically diseases, as ischemic heart disease (observed in elderly adults). In 2009–2011 were noted deaths of pregnant women with lesions of placenta and fetuses. In 2011 death of 31 ys healthy man occurred on the 35th day of illness clinically regarded as influenza with bacterial superinfection. The results of postmortem investigations proved that clinically diagnosed infections were expressed weakly, but provoked the activation and severe course of respiratory chlamydiosis, proved by histopathology, IHC and electron microscopy.
Conclusion: Immediate death causes in influenza are quite different and have to be taken in consideration.

PS-04-011
A rare case of tuberculosis within Warthin's tumour in the parotid gland
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Objective: Tuberculosis in the parotid gland is rarely encountered even in endemic countries. It accounts for 2.5–10 % of parotid gland lesions. The coexistence of tuberculosis with Warthin's tumour (WT) is extremely uncommon and very few cases have been reported in the literature. We report a new case of a WT associated with tuberculosis in order to discuss the possible mechanisms of this association.
Method: The histological features of this association are described with a review of the related literature.
Results: A 53-year-old man, with no personal history of tuberculosis, presented with a right parotid mass measuring 4.5 cm. An exofacial parotidectomy with a lymph node biopsy were performed. Frozen section of the parotid mass concluded to WT. Paraffin sections confirmed this diagnosis and revealed the presence in the lymphoid stroma of multiple epithelioid granulomas with caseous necrosis. Histological examination of the lymph node revealed epithelioid granulomas without necrosis. Further clinical and radiological investigations didn't show another location of tuberculosis. The patient was successfully treated with anti-tuberculosis drugs.
Conclusion: To explain the association of WT with tuberculosis, some authors suggested that the lymphoid stroma of the WT can behave as a regional lymph node. Therefore, it can be affected with tuberculosis like any other lymph node.

PS-04-012
Seasonality of community-onset Acinetobacter baumannii isolation
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Objective: Seasonal and temperature-associated features of Acinetobacter baumannii isolations from hospitalized patients have been reported. In this study, we evaluated trends in community-onset A. baumannii isolations and variability according to temperature, which could provide insight into strategies to control A. baumannii infections in Korea.
Method: We compared numbers of A. baumannii complex (A. baumannii, Acinetobacter nosocomialis, Acinetobacter pittii, and Acinetobacter calcoaceticus) cases per month, which were converted to cases per 100,000 admissions for hospital-acquired isolates, and cases per 1,000 outpatients for community-onset isolates collected between the warm season (≥20 °C average mean temperature) and the cold season (<5 °C average mean temperature). Clonal relatedness was evaluated with pulsed-field gel electrophoresis (PFGE) using the SmaI restriction enzyme on randomly selected isolates, which were confirmed as A. baumannii.
Results: The median number of community-onset A. baumannii complex cases was 13.8 (interquartile range, IQR: 9.5–17.6) in warm months and 10.1 (IQR: 6.3–13.2) in cold months (p-value = 0.0002). There was a positive correlation between community-onset A. baumannii complex cases and temperature (Pearson's r = 0.6805, p-value = 0.0149). Using a cut-off threshold of 80 % similarity, healthcare-associated isolates were clustered in similar groups, whereas community-onset isolates showed a variety of band patterns in a pulsed-field gel electrophoresis analysis.
Conclusion: We identified a pattern of seasonality for community-onset A. baumannii complex isolations, but not for healthcare-acquired isolations. The latter were highly clonal and affected by outbreaks rather than by natural selection.

PS-04-013
Strongyloides hyperinfection syndrome
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Objective: Strongyloides stercoralis (strongyloidosis) is an intestinal nematode which is usually asymptomatic in a healthy host, however, in an immunocompromised patient where hyperinfection is associated with disseminated disease it may become a life threatening condition.
Method: Although S. stercoralis is often considered to be a disease of tropical and subtropical areas, several autochronous infections were reported also from areas with moderate climate (e.g. central Europe). The term hyperinfection describes the syndrome of an accelerated autoinfection, which is generally the result of an altered immune status.
Results: The standard examinations for strongyloidosis include techniques for detection of the larvae in stool specimens and assays focused on detection anti-S. stercoralis antibodies. The final diagnosis is based on histopathological findings of the parasites in tissue biopsies.
Conclusion: Here we report 3 cases of S. stercoralis hyperinfection. Two cases were diagnosed in immunocompromised patients from bioptic samples of small intestine and in one case the diagnosis was established post mortem at autopsy. Our results showed, that also in a nonendemic areas of Central Europe strongyloidosis can develop and when left untreated, can lead to life-threatening disease under certain circumstances.

PS-04-014
Pathologic features of chronic calculous cholecystitis with microbial dysbiosis identified by bile juice metagenomic sequencing
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Objective: The normal bile has been believed sterile, and the role of infection in gallbladder (GB) cancer has been mostly studied by epidemiologic perspective. The global microbiome of bile juice and its association with GB diseases was not investigated yet.
Method: We performed metagenomic sequencing on bile samples from ten healthy individuals, 14 patients with GB diseases, including chronic calculous cholecystitis (CCC), acute cholangitis and cancer. The clinicopathological characteristics were compared between CCC with normal and dysbiotic microbiome patterns.
Results: All normal bile samples were consistently composed of six major genera: Pseudoalteromonas, Vibrio, Aeromonas, Cetobacterium, Propionibacterium, and Gamaproteobacteria. Bile juice microbiome from patients with GB diseases dominated by Enterobaceriacea. Especially, Citrobacter was abundant in bile from GB cancer and a subset of CCC. CCC with dysbiosis showed marked epithelial atypia, severe active inflammation with wall thickening, and large gallstones (>3 cm), whereas CCC with

normal microbiome pattern revealed mild chronic inflammation without any active lesion. On immunohistochemical staining, CCC with dybiosis showed focal p16 expression, weak membranous EGFR and HER2 expression, and higher Ki-67 labelling. However, CCC without dysbiosis showed negative expressions of p16, EGFR and HER2 with low Ki-67 labelling. No KRAS mutation was identified in both groups.
Conclusion: We identified normal flora in bile juice of healthy individuals and demonstrated association of dysbiosis with GB diseases. The histologic findings and immunohistochemical results also can support that dysbiosis may be associated with chronic active lesion with epithelial atypia, which can lead to develop precancerous or malignant lesion.

Sunday, 3 September 2017, 09:30–10:30, Hall 3
PS-05 Pulmonary Pathology

PS-05-001
Is peritumoural lymphocyte infiltration predictor for PDL-1 positive patients with locally advanced or metastatic non-small cell lung cancer (NSCLC)?
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Objective: Tumour programmed death ligand one (PD-L1) which is the ligand for programmed death receptor-1 (PD-1); the expression of PD-L1 on a target cell binding to PD-1 can inhibit T-cell receptor signaling and diminish interactions with dendritic cells, resulting in anergy. Immune checkpoint inhibition has shifted treatment paradigms in non-small cell lung cancer (NSCLC). T regulatory cells play important roles in immune suppression, the reversal of which is vitally important for the success of immune therapy. Conflicting results have been reported regarding the immune infiltrate and programmed death-ligand 1 (PD-L1) as a prognostic marker. We correlated the peritumoural immune infiltrate and PD-L1 expression with clinicopathologic characteristics of resected with locally advanced or metastatic NSCLC
Method: Tumour slides of surgical specimens of 50 cases with lung cancer diagnosed in our department from 2012 to 2016 were analyzed retrospectively. Immunohistochemistry was performed for PD-L1. Strong PD-L1 expression was defined as greater than 50 % tumour cell positivity.
Results: The mean age was 59,6 years. 12 were female and 38 were males. Of 50 patients, 15 were node-negative (N0), 2 N1 and 23 N2; 10 N3 34 were adenocarcinomas (AC), 11 squamous cell cancers (SCC) and 5 other. Strong PD-L1 expression was found in 18 % cases and weak PD-L1 expression was found in 28 % cases. Strong peritumoural lymphocytes infiltration was found in 24 % cases. PD-L1 expression was not associated with peritumoural lymphocyte statistically.
Conclusion: PD-L1 expression and peritumoural lymphocytes were not concordant in our study.

PS-05-002
Investigations on hematoxylin & eosin stained sections of acinar pulmonary adenocarcinoma by confocal laser scanning microscopy
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Objective: Lung cancer is the most common form of cancer in the world. Imaging techniques such as Confocal Laser Scanning Microscopy (CLSM) or Multiphoton Laser Scanning Microsopy (MLSM) can alleviate part of the problems associated to conventional imaging techniques, and in certain cases can eliminate the need for tissue removal. We attempt to contribute in this regard by discussing a series of data sets collected on H&E-stained sections of Acinar Pulmonary Adenocarcinoma by Bright Microscopy (BM) and CLSM.
Method: We employed a correlative imaging approach in which H&E stained lung tissue sections were imaged with BM and CLSM. BM images have been collected using a Leica DM3000 system, while Confocal Laser Scanning Microscopy data sets were acquired using a Nikon C2+ system working in fluorescence. For excitation a 488 nm laser beam was used.The tissue was formalin-fixed and paraffin-embeded.
Results: A series of analogies were established between the BM and CLSM images. In CLSM images the neoplastic proliferation is delineated by distinct borders consisting in fibrous bright septae. At closer magnification, the acinar adenocarcinoma with gland formation and the nuclear contours are well defined.
Conclusion: CLSM and MPM provide the possibility to non-invasively acquire in-focus images from selected depths from living, fixed and frozen specimens.

PS-05-003
Comparison of PD-L1 mRNA expression measured with the CheckPointTyper® assay with PD-L1 protein expression assessed with immunohistochemistry (IHC) in lung cancer (NSCLC)
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Objective: PD-L1 evaluation in NSCLC became important since development of anti-PD-L1/PD-1 drugs. Comparison of trials investigating prediction of response to these drugs is complicated due to different PD-L1 antibodies and cut-offs used. We analyzed comparability of PD-L1 mRNA and protein expression and dependency on the way of tissue acquisition.
Method: Prospectively, $n = 22$ NSCLC cases ($n = 9$ EBUS TBNA, $n = 5$ metastases) were evaluated for PD-L1 protein on tumour cells (TC) and immune cells (E1L3N, Cell Signalling; 28-8, Abcam) and PD-L1 mRNA (CheckPoint TYPER® assay, STRATIFYER).
Results: In primary NSCLC ($n = 17$), PD-L1 mRNA and 28-8 TC IHC agreement was excellent (Kappa value = 0.85, p-value = 0.0002). In EBUS-TBNA ($n = 8$), PD-L1 mRNA expression showed perfect agreement with 28-8 antibody (Kappa value = 1.0, p-value = 0.0023). In metastases, differences between PD-L1 mRNA and protein became apparent (Kappa 0.2; p-value 0.2525). However, PD-L1 mRNA significantly differed when comparing 28-8 TC staining of tumours >49 % with 1–49 % and 0 % ($p = 0.0040$; $p = 0.0081$, respectively).
Conclusion: PD-L1 mRNA (CheckPoint TYPER®) and 28-8 protein staining showed excellent agreement in primary NSCLC including lymph node biopsies. Metastatic lesions require cut-off adoption according to tissue type. PD-L1 protein expression in >50 % tumour cells by 28-8 antibody can be reliably detected by RT-qPCR from non-macrodissected primary NSCLC tumour samples.

PS-05-004
Adequacy, clinicopathological and service parameters of molecular testing on respiratory cytology specimens at a UK Tertiary Referral Centre: A review of 64 cases from 2013 to 2016
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Objective: Next generation sequencing (NGS) and ALK FISH are becoming routine practice for respiratory cytology specimens in identifying actionable driver mutations, which is crucial in the management of metastatic lung cancer. We aim to assess our local specimen adequacy rates and turnaround time from 2013 to 2016.

Method: Retrospective observational study. 64 out of 406 (15.8 %) cases were sent for molecular analysis. All cases were deemed sufficient by cytopathologists. The most common test platform was a 50-gene NGS panel (Ion AmpliSeq Cancer Hotspot Panel, Thermo Fisher) (81 %, 52/64). ALK FISH was performed in 88 % (56/64) of cases. Demographic and clinicopathological data were retrieved from our laboratory information management system.
Results: The majority of cases were adenocarcinoma (89 %, 57/64) and 80 % (51/64) were stage III/IV. Median cellularity was 50 %. The adequacy rates for NGS and ALK FISH were 98.4 % (62/63) and 94.6 % (53/56) respectively. EGFR mutations, ALK rearrangement and BRAF mutations were detected in 12.7 % (8/63), 5.4 % (3/56) and 3.3 % (2/60) of cases. The median time from procedure to molecular test report was 23.5 days.
Conclusion: This is a pilot study demonstrating satisfactory specimen adequacy rates at our centre. The substantial time to molecular test results represents areas for service improvement.

PS-05-005
Recurrence of Langerhans cell histiocytosis in pulmonary allograft - a case report
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Objective: Langerhans cell histiocytosis is seldomly accounted as underlying pathology for deterioted lung function resulting in lung transplantation and there are only few case reports of recurrence of Langerhans cell histiocytosis in pulmonary allografts.
Method: We herewith report a case of recurrent Langerhans cell histiocytosis in pulmonary allograft in a 46 year old male patient.
Results: Recurrent disease was diagnosed clinically and was confirmed histologically 2 years after lung transplantation. The patient was a former smoker, ceased smoking before lung transplantation according to requirements for listing for lung transplantation and admitted to have restarted smoking following lung transplantation. The patient was strongly advised to quit smoking.
Conclusion: Our case confirms that smoking may trigger recurrence of Langerhans cell histiocytosis in pulmonary allografts.

PS-05-006
Transbronchial biopsy utility diagnosing interstitial lung diseases: Revision of 243 cases
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Objective: The utility of Transbronchial biopsy for the diagnosis of interstitial lung diseases have been questionated. Nowadays, the introduction of criobiosy makes necessary and evaluation of both methods. We continue using transbronchial biopsy as the main method to diagnose interstitial lung diseases and our objective is to prove its utility.
Method: We revised 243 transbrochial biopsies between 1996 and 2013. We analized the clinical, radiologic, histological and final diagnosis.
Results: In 86 of 243 (34 %) we obtained a direct diagnosis, in 69 (28 %), the histology was compatible with the clinical diagnosis, in 63 (26 %) histology was helpful to obtain the final diagnosis and 29 were not valuable biopsies (11 %). The diagnosis was possible in 64 % of usual interstitial pneumonia cases confirmed in which a tranbronchial biopsy was made, in 94,4 % of Non specific pneumonias, in 96 % of Organized penumonias and in 100 % of respiratory bronchiolitis.
Conclusion: We saw that the utility of transbronchial biopsy to make a succesful diagnosis in interstitial lung diseases was 88 %, with a direct diagnosis or adding up helpful information to obtain a final diagnosis.

PS-05-007
Coexistence of lung adenocarcinoma and melanoma in the same pleural metastatic focus - a case report
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Objective: Coexistence of different malignant neoplasms in the same metastatic focus is extremely rare.
Method: A case of a 66-year-old male with a history of nodular melanoma of the left leg is presented. The patient had on CT imaging a tumour at the inferior lobe of the right lung, measuring 4,5 cm, with satellite nodules, a smaller tumour at the right lobe of the liver, measuring 1,5 cm, as well as enlarged left inguinal lymph nodes. All the above tumours were regarded as metastatic melanoma foci. A parietal pleural nodule was resected via video-assisted thoracoscopic surgery (VATS).
Results: Histological and immunohistochemical features of the resected specimen showed coexistence of lung adenocarcinoma (TTF-1+) and melanoma (Melan-A+) at the same pleural nodule.
Conclusion: Coexistence of two or more primary malignancies in the same individual is a well-known phenomenon. However, the presence of histologically distinct malignancies in the same metastatic focus is extremely rare. To our knowledge, this is the first case where lung adenocarcinoma and melanoma, two tumours with different histogenesis and tumourigenic pathways, coexist as a mosaic or have “collided” in the same metastatic focus at the parietal pleura. The value of immunohistochemistry in discerning the two neoplastic components is emphasized.

PS-05-008
Salivary gland type tumours of lung and tracheobronchial tree: Experience from a tertiary care cancer centre of India
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Objective: Clinicopathological features of a Primary pulmonary salivary gland type tumour(PPSGT) are uncommon intra-thoracic neoplasms was studied.
Method: Retrospective search of the pathology database over a period of 13 years (between 2003 to 2016) revealed 192 cases of salivary gland type tumours involving the lung.Out of these 141 cases were excluded as they were metastatic to lung based on clinico-radiological features. Hence 51 cases of PPSGT formed the study group.
Results: Out of the total 51 cases of PPSGT, only one was benign, rest all[50 (98 %}) were malignant. Tumour was centrally located in 46 cases(90.2 %),while 5 cases(9.8 %) had peripheral mass. The mean age of presentation was 47.9 years with male predominance(M: F ratio = 1.6:1).Thirty-five(68.6 %)patients were non- smokers. The tumour size ranges between 2 and 4 cms in 33/51 cases, and was >4 cms in 12 cases. On histopathologic examination; 20/51 cases(39.2 %) were of mucoepidermoid carcinoma(MEC), 15/51(29.4 %) were of adenoid cystic carcinoma (ACC), 08/51(15.6 %) of epithelial myoepithelial carcinoma(EMC) whereas the rest 8/51(15.6 %) had varied histological subtypes. Surgical excision was the done in 31 cases. The overall survival was related to the stage of the disease, histological grade and performance status.
Conclusion: MEC are the most common type of PPSGT followed by ACC; other types being exceedingly rare. Diagnosis can be challenging in small biopsies, however distinction from primary lung carcinomas is imperative.

PS-05-009

Correlation between pathological and molecular features in Non Small Cell Lung Cancers (NSCLC) and PD-L1 testing: Our experience

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Objective: Recent advances in the treatment of NSCLC show Programmed Death Ligand 1 (PD-L1), the ligand for the inhibitory Programmed Death receptor 1 (PD-1) checkpoint as one possible biomarker for selecting patients likely to benefit from immunotherapy. PD-L1 immunohistochemistry has been successfully identified in such patients. We reviewed our data regarding PD-L1 IHC 22C3 pharmDx.
Method: We retrieved all cases of lung cancer tested for PD-L1, we reviewed histological diagnosis, molecular and cytogenetic results andPD-L1 status.
Results: We tested 80 cases of NSCLC, 50 males and 31 females (age range: 42 to 84). Fifty-two (65 %) cases were non-mucinous adenocarcinomas, 6 (0.7 %) were mucinous adenocarcinomas, 17 (21 %) squamous carcinomas and 5(0.6 %) were other subtypes. Thirty-seven adenocarcinomas (64 %) showed predominant solid pattern. ALK rearrangement was present in one case whilst 3 (3.75 %) showed EGFR actionable mutations. Six (7 %) cases were inadequate, 23 (31 %) negative, 18 (24 %) weak positive and 33 (45 %) strong positive being suitable for treatment. Chi square test showed no significant correlation between histology and PD-L1 expression ($p = 0.33$) however 19(57.6 %) of strong positive cases were adenocarcinoma with solid pattern.
Conclusion: Our series show that patients with adenocarcinoma with solid pattern are more likely to express PD-L1 and be eligible for immunotherapy.

PS-05-010

Adjuvant treatment and survival in TNM-7 pT3N0M0 non-small cell lung cancer in The Netherlands: A support for including histology to staging

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Objective: The aim of this study was to analyse the frequency distribution and outcome of various subgroups in T3N0M0 NSCLC cases in the Netherlands over a period from 2010 to 2013.
Method: From the Netherlands Comprehensive Cancer Organisation (IKNL) anonymized data of NSCLC patients were retrieved from the period 2010–2013. The data of pathologic T3N0 cases were coupled with the nationwide network and pathology registry in the Netherlands (PALGA), according to the 7th edition of the cancer staging manual of AJCC.
Results: 505 pT3N0 lung resection cases were retrieved: > 7 cm: $n = 174$ (34 %); two or more tumours in the same lobe: $n = 148$ (29 %); parietal pleural invasion: $n = 132$ (26 %); > 7 cm and pleural invasion: $n = 47$ (9 %); location within 2 cm of the carina: $n = 2$ and organizing pneumonia (OP) or atelectasis of the lobe: $n = 2$. Statistical analysis showed a significantly better prognosis i) for the 2nd nodule T3N0 subtype compared to the other subtypes ($p = 0.002$); ii) for adenocarcinoma (AdC) versus squamous cell carcinoma (SqCC; $p = 0.034$) and NSCLC NOS ($p < 0.001$).
Conclusion: The prognosis within pT3N0M0 is heterogeneous. A better prognosis was found for the 2nd nodule T3N0 subtype. Comparing histological subtypes, AdC had a better prognosis compared to SqCC and NSCLC NOS, supporting the inclusion of histological subtypes in the pTNM staging.

PS-05-011

Eukaryotic translation initiation factors impact non small cell lung cancer

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Objective: Non small cell lung cancer (NSCLC) is the leading causes of cancer related death worldwide. Deregulation of protein synthesis has received considerable attention as a major step in carcinogenesis. Eukaryotic initiation factors (eIFs) play a crucial role in translation and ensure the correct 80S ribosome assembly. eIFs are linked to the MAPK and the mTOR signalling cascades, which have become major targets in cancer therapy. We hypothesized that eIFs represent an interface for carcinogenesis in lung cancer.
Method: Paired NSCLC and non neoplastic lung tissue from 28 patients was analyzed on RNA and protein level for eIFs and mTOR pathway member expression by qPCR and Western blotting. Additionally paired NSCLC and NNLT from 400 individuals were studied by immunohistochemistry on tissue micro arrays.
Results: Western Blot and mRNA analysis of NSCLC revealed significant up-regulation of the eIF subunits p2α, 2α, 1A, 4A, and eIF6 compared to NNLT ($p < 0,05$). Immunohistochemistry demonstrated a higher staining intensity in neoplastic cells for the subunits eIF2α, eIF4E and eIF3H compared to controls.
Conclusion: Our data indicate that eIFs are significantly upregulated in NSCLC, suggesting an important component in lung carcinogenesis. A better understanding of the underlying molecular mechanisms might contribute to the development of novel treatment strategies.

PS-05-012

PD-L1 expression in different samples of non-small cell lung cancer

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Objective: PD-L1 is a predictive biomarker for immunotherapy, which requires assessment of PD-L1 expression. The aim was to evaluate adequacy of histology and cytology samples for PD-L1 testing.
Method: 307 samples (208 biopsies, 41 resection and 58 cytology) from 276 patients were stained for PD-L1. Methanol-fixed cytospins and FFPE sections stained with PD-L1 mouse monoclonal antibody (clone 22C3, Dako, Denmark) on automated staining platform (Benchmark, Roche, USA). 17 and 12 patients had cytology/biopsy and biopsy/resection specimens, respectively. PD-L1 expression was evaluated on tumour cells. Samples containing 100 or more tumour cells were considered representative. PD-L1 positivity was defined by cutoff values of 1 % and 50 %.
Results: With cutoff value of 1 %, 53 % patients were positive for PD-L1. We found 59,4 % adenocarcinomas, 32,9 % SCC, 6,1 % NSCLC-NOS, 0,7 % LCNEC and 0,7 % adenosquamous carcinomas. 74 % cytology samples were PD-L1 positive. With cutoff values of 1 and 50 , 47 and 21 % biopsies were PD-L1 positive, respectively. Resection specimens were PD-L1 positive in 39 and 17 %, using cutoff values of 1 and 50 %, respectively. Patients with cytology/biopsy and biopsy/resection specimens showed 77 and 100 %, respectively.
Conclusion: All types of cytology and histology samples included in our study were adequate for evaluation of PD-L1 expression in tumour cells of NSCLC.

PS-05-013

Identification of morphologic parameters affecting the prognosis of lung squamous cell carcinoma patients by computer-based morphometric analysis

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Objective: In addition to staging, morphological features may bring additional criteria to stratify patients into relevant prognostic groups. The objective of our study was to identify morphological features of lung squamous cell carcinoma (LSCC) with prognostic relevance, using an image-based computational method on histologic sections.
Method: Three patients' cohorts of surgically resected lung SCC tumours were investigated (tissue microarray (TMA): n = 208, whole sections (WS): n = 99). TMA and WS cohorts were immuno-histochemically stained with pan-cytokeratin. Color-based segmentation followed by morphologic features screening were performed. The parameter tumour fragmentation (TF), defined as tumour clusters >800 μm2 (circa >5 cells) was further evaluated. An external validation TCGA (The cancer genome atlas) cohort (n = 335, H&E stained) was scored by eye for TF.
Results: We identified tumour fragmentation (TF) as a morphologic feature associated with poor outcome, independent from tumour stage, in two independent clinical cohorts. This was confirmed using a similar human-based scoring system in the TCGA cohort.
Conclusion: In conclusion, by using a computer-based morphometric approach, we identified TF as a new independent prognostic marker for chemotherapy-naïve LSCC patients, which could serve to refine current tumour grading systems.

PS-05-014

Diagnostic significance of the signal distance cut-off value in ALK-EML4 rearranged lung cancer

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Objective: Detection of ALK-EML4 rearrangement by FISH can be challenging as the physical distance between these genes is very short. Split distances of the rearranged 3′-red and 5′-green ALK signals are often less than the requested two-signal diameters apart. Our aim was to examine the diagnostic significance of the signal-distance cut-off value.
Method: Tissue samples from 166 KRAS/EGFR double wild-type lung adenocarcinoma were investigated by using ZytoLight ALK/EML4 TriCheck FISH. ALK rearranged signal pattern was evaluated by using both ≥1 and ≥2 signal-diameter cut-off for ALK 3′–5′ split signal. Involvement of EML4 was detected by red-aqua signal fusion. ALK positivity was determined by proportion of rearranged cells using a cut-off value of 15 %.
Results: By using ≥1 signal-diameter cut-off, 13/166 ALK rearranged tumours were found with involvement of EML4 in seven of them, including 5′-green deletion signal pattern in 2/7. By using ≥2 signal-diameter cut-off protocol, two of the five ALK-EML4 rearranged red-green signal split cases were detected as ALK-negative (10 % [instead of 62 %] and 12 % [instead of 52 %] rearranged cells, respectively) while ALK rearrangement status remained unchanged in all other cases.
Conclusion: Using the ≥2 signal-diameter cut-off protocol in ALK-EML4 rearranged cases can lead to false negative results.

PS-05-016

Clinicopathological analysis of PD-L1 expression in invasive non-small cell lung cancers

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Objective: Recently, immune checkpoint inhibitory approaches have shown considerable promise as innovative effective therapies for cancer patients. For lung cancers, especially non-small cell lung cancers (NSCLCs), two immune checkpoints, PD-1 and PD-L1, have emerged as important targets for immunotherapy. Our aim is to correlate immunohistochemical (IHC) expression of PD-L1 with clinicopathological parameters in NSCLC.
Method: We examined 99 cases of invasive NSCLC, including 41 squamous cell carcinomas (SCCs) and 58 adenocarcinomas (ADCs), resected in our institution for a recent 2-year period. One representative histologic section of each case was immunostained with anti-PD-L1 antibody. The extent of immunoreactive tumour cells and infiltrating intratumoural lymphocytes was respectively scored in a semiquantitative fashion. The proportion score (PS) was statistically correlated with multiple clinicopathological parameters. In addition, for the purpose of dichotomization, immunoreactivity seen in > 1 % of tumour cells was considered IHC "positive".
Results: PD-L1 PS was significantly higher in SCCs than in ADCs (p = .0154), and 56.1 and 32.8 % IHC "positive" cases were found, respectively. In addition, the same was true in intratumoural lymphocytes (p = .0125). There was a positive correlation between the pathologic stage and IHC PS (p = .0131). No correlation was found between PS and gender, PS and age, PS and tumour size, or PS and lymphovascular invasion status (i.e., present or absent).
Conclusion: PD-L1 expression was more significantly seen in higher pathologic stages of NSCLC cases, which might be associated with tumour immune evasion. This finding further supports the fact that the anti PD-1/ PD-L1 therapy could be of potential use in immunotherapy for patients with advanced NSCLC.

PS-05-017

Telomere shortening in type II pneumocytes relates to fibrotic areas in idiopathic pulmonary fibrosis and has a detrimental effect on survival

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Objective: We quantified telomere length (TL) in type II (AT2) pneumocytes, of sporadic and familial idiopathic pulmonary fibrosis (IPF) lung tissue. Furthermore, survival analysis was performed.
Method: Lung FFPE slides were stained using telomere Fluorescence In Situ Hybridization (FISH). Subsequently, quantification of telomere fluorescence was measured per cell type, discriminating between AT2 and surrounding cells in non-fibrotic and fibrotic areas. Quantitative polymerase chain reaction (qPCR) was used for whole lung biopsy TL measurements.
Results: For sporadic IPF patients, AT2 cell TL in non-fibrotic areas was 2.24 times longer than in fibrotic areas (p < 0.001). In familial patients carrying a telomerase (TERT) mutation, AT2 cell TL was shorter than in sporadic patients (p = 0.02). However, no difference in surrounding cell TL was observed between non-fibrotic and fibrotic areas of both sporadic and TERT subjects (p = 0.67). Finally, we found that IPF patients with shortest lung biopsy TL had a shorter survival (22 months) compared to patients with long TL (survival 63 months, p = 0.003).

Conclusion: The co-localisation of short telomeres in AT2 cells in fibrotic areas of IPF lung suggests that telomere shortening plays a critical role in the fibrotic remodeling in IPF. Furthermore, short lung telomere length has a detrimental effect on survival.

PS-05-018

Effective PD-L1 pathologist training across the dynamic range using an innovative digital training platform

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Objective: To address challenges in pathologist training for multiple PD-L1 indications, each with unique therapeutic cut-off, a universal training method for scoring tumour cell membrane staining with VENTANA PD-L1 (SP263) Assay (SP263 Assay) was developed utilizing an innovative digital training platform.
Method: Training of 19 international pathologists was conducted for IHC staining interpretation with the SP263 Assay using FFPE NSCLC cases representative of the dynamic range of staining on a digital training platform. Training consisted of: didactic presentation on SP263 Assay characteristics, guided cases(12), self-study cases(11), and assessment cases(30). An acceptable range for scoring accuracy was informed by pilot data collected from a preliminary training session. Accuracy was determined by comparison to the acceptable range.
Results: One hundred percent of trainees passed with accuracy scores > 90 %, and with average scores for 29/30 assessment cases within ±7 of consensus. The 19 trainees showed ≥ 90 % accuracy using universal percentage scoring when assessment test cases were categorized as positive or negative at various cut-offs: 1 , 5 , 10 , and 50 %.
Conclusion: Universal training on interpretation of staining by the SP263 Assay across the dynamic range of PD-L1 tumour cell expression on NSCLC samples utilizing a digital training platform provides a robust, accurate and successful approach to pathologist training, and flexibility around the changing landscape of therapy cut-offs.

PS-05-019

Is diffuse idiopathic pulmonary neuroendocrine cell hyperplasia an exclusive disease of women in our region? Report of six cases, all in women

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Objective: To review the clinical, radiological and morphological features of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH), an infrequently reported disease.
Method: We reviewed the clinical, radiological and pathological data of six cases diagnosed as DIPNECH between 2010 and 2017 at our Institution.
Results: Patients age ranged from 57 to 76 years old. Three out of six were incidental findings discovered on X-rays, two were found during follow up for a malignant disease (one case had a co-existing colorectal metastases) while the last one had a clinical history of pleural effusion. Radiologically four of them were suspicious for metastatic disease (presented as multiple pulmonary nodules) whereas the other two were suspicious of primary lung cancer (presented as spiculated masses). Two lobectomies and four wedge biopsies were performed consequently. Regarding the morphological features, multiple nests of monomorphic and sometimes spindle cells were discovered associated in four cases to carcinoid tumours. Neuroendocrine cell proliferation was confirmed with immunostains for chromogranin, CD56 and synaptophysin. All the patients have had an indolent course without treatment
Conclusion: DIPNECH is a rare and clinically or radiologically unsuspected disease, most prevalent in women which diagnoses relays on microscopic findings. Its prognosis is excellent.

PS-05-020

Pleomorphic mesothelioma: Report of a rare case with emphasis on differential diagnosis

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Objective: According to the 2015 WHO classification, pleomorphic mesothelioma is a rare, poor prognostic subtype of epithelioid diffuse malignant mesothelioma, which is composed of highly pleomorphic epithelioid cells with prominent cytologic atypia and frequently multinucleation, thus mimicking a pleomorphic carcinoma.
Method: The patient, a 66-year-old man, presented with diffuse pleural nodularity, multiple intrapulmonary nodules in the right lung and enlarged regional lymph nodes. The superior segment of the right lower lobe with an intrapulmonary nodule, measuring 2,2 cm in maximum diameter, as well as parts of the pleura were resected.
Results: Histological and immunohistochemical features of the resected specimens were consistent with pleomorphic epithelioid mesothelioma.
Conclusion: Pleomorphic mesotheliomas can be confused with a variety of tumours with similar morphology, mainly pleomorphic carcinoma of the lung, anaplastic thyroid carcinoma and pleomorphic sarcomas. The immunohistochemical profile, including variable expression of common mesothelial markers, such as calretinin, WT1, podoplanin, mesothelin and keratin 5/6, can be very helpful in discerning these entities. Pleomorphic mesothelioma is associated with aggressive clinical and biological behaviour, similar to that of biphasic and sarcomatoid mesotheliomas, so its recognition can significantly affect the treatment and prognosis of the patients.

PS-05-021

Trends in lung cancer incidence by histologic subtype in the northeastern city of Brazil, 2013–2015

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Objective: To identify the histopathological characteristics in patients with lung cancer (LC) as well to describe distribution of the epidemiological profile in a Brazilian sample.
Method: Retrospective cross-sectional study with inclusion of 781 pacients with histologically confirmed LC in Messejana Hospital Dr Carlos Alberto Studart, Fortaleza city, Brazil, between 2013 and 2015.The slides were reviewed by a pneumopathologist and two general pathologists.
Results: In the study, the mean age was 64.5 + 11.0 SD years. The trend over the period was lowest in 2013 (n = 212) and highest in 2015 (n = 280). The most frequent age group was 65–79 years (43.7 %) with predominance of female patients (50.7 %). The histological subtype more frequently was non-specified adenocarcinoma (26.5 %), low differentiated carcinoma (11.1 %), small cells carcinoma (9.5 %) and squamous cell carcinoma (8.3 %). In females, LC incidence increased over the entire study period by +15,5 % per year; this trend was mainly in the age group 65–79 years (n = 170) and by adenocarcinoma incidence (n = 102).

Conclusion: Female LC incidence rates have increased in brazilian sample and the same tendency was observed in literature between 1996 and 2011. These trends may reflect a better understanding of the risk factors and may impact the preventive measures to be implemented at the community level.

PS-05-022

Study of CDKN2A and p16 in malignant pleural mesothelioma in relation to asbestos exposure

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Objective: Objective: We studied the copy number of CDNK2A and the corresponding protein expression (p16) and their relation to asbestos exposure in 46 malignant pleural mesotheliomas (MM) from patients with different asbestos-burdens.
Method: Methods: DNA copy numbers were detected by fluorescence in situ hybridization using dual color probe mix for CDKN2A and centromere #9, p16 expression was studied by immunohistochemistry. Asbestos fiber burden in lungs was determined from ashed lungs with electron-microscopy.
Results: Results: In patients with low asbestos-burden (0–0.5 million fiber/gram dry lung tissue, f/gdlt), the CDKN2A copy numbers in MM tissue were abnormal in 71 % of cases and four patients stained positively for p16 in MM tumour tissue. In 37 patients with high asbestos burden (>1 million f/gdlt, median 8.9 million), the CDKN2A copy numbers in MM tissue were changed in 97 % of the cases. Six out of 37 stained positively for p16 in mesothelial cells. Twelve patients with high asbestos-burden had some p16 staining in the stroma, but not in the malignant mesothelial cells, none in the low asbestos-burden group stained in this way.
Conclusion: Conclusion: No significant differences were found in CDKN2A status in relation to asbestos-burden. Intriguingly stromal p16 positivity was found to relate to high exposure.

PS-05-023

Synchronous primary pulmonary tumours

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Objective: Synchronous primary pulmonary tumours are defined as the simultaneous occurrence of two or more primary pulmonary carcinomas of different histologic types, regardless of localization, or multiple nodules with similar histologic type if they are in different segments, lobes, or lungs. This definition accounts for 0.26–1.33 % of reported tumours, which are usually composed of several histologic types, being squamous cell carcinoma one of the most frequent.
Method: 75-year-old male with surgically excised oral carcinoma in 1999, treated with radiotherapy, now underwent right superior lobectomy and lymphadenectomy after core biopsy diagnosis of adenocarcinoma.
Results: The analysis of the surgical specimen confirms adenocarcinoma, papillary predominant pattern, with hilar lymph node metastases and uninvolved margins and visceral pleura. Additionally, a 0.9 cm nodule of squamous cell carcinoma was identified on bronchus sections, associated with high-grade dysplasia and involved lymph nodes and bronchial margin.
Conclusion: Confronted with the rareness of finding two tumours in the same pulmonary lobe, and taking the patient's history into account, one might think that the squamous lesion could correspond to a metastasis of the oral carcinoma. Nevertheless, the association of an infiltrative component with high-grade intraepithelial dysplasia, together with its endobronchial location, would suggest synchronous primary pulmonary tumour as the main diagnostic possibility.

PS-05-024

Could efflux pumps P-gp, MRP1 and BCRP have predictive and prognostic value for the neoadjuvant chemotherapy in patients with non-small cell lung carcinoma

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Objective: Lung cancer is the most common cause of neoplasia-related death worldwide. Although surgical resection is the most favorable treatment for patients with non-small cell lung carcinoma (NSCLC), relapse is still high, so neoadjuvant chemotherapy (NAC) is an accepted treatment modality.
Method: We investigated whether efflux pumps P-gp, MRP1 and BCRP proteins could have predictive and prognostic value for the NAC application in two groups of NSCLC patients, those who received and those who did not receive NAC.
Results: MRP1 expression is significantly higher in patients who did not receive NAC, which means that they had intrinsic resistance to chemotherapy. Also, MRP1 is significantly higher in patients who did not receive NAC and had I or II stage of the disease. BCRP was significantly higher in patients who did not receive neoadjuvant chemotherapy and were without lymph node invasion. Patients who did not receive NAC and had lower P-gp expression lived significantly longer than patients who received this therapy and had the same P-gp expression. Besides, patients with SCC, without NAC and with lower P-gp expression lived significantly longer than patients with NAC.
Conclusion: Efflux pumps P-gp, MRP1 and BCRP could have predictive and prognostic value for the NAC in patients with NSCLC and could be used in personalized therapy.

PS-05-025

Multiple nodular lesions on CT: Epitheloid hemangioendotheliomas in lung

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Objective: Epitheloid hemangioendothelioma (EHE) is a rare and potentially challenging entity on frozen sections.
Method: Thirty-nine years old female patient had hemoptysis. CT imaging represented multiple small and bilateral nodular lesions. She underwent surgery.
Results: A 0,5 cm nodule with irregular borders in the lung parenchyma was sent for intraoperative consultation. On frozen section, small epitheloid cells were seen on a vascular background. Some of the epitheloid cells were forming clusters in the alveolar spaces.We reported the lesion as a nodular lesion with unknown malignant potential, to the surgeon. Left upper lobectomy was performed. Macroscopically, there were multiple tan-white colored nodules with a maximum diameter of 0,5 cm and irregular borders. Microscopically, the nodules consisted of small epitheloid cells which formed clusters, vascular structures in a myxoid-chondroid background. The epitheloid cells had vacuole-lumen like empty spaces- in their cytoplasm. Vascular structures of various sizes

contained erythrocytes in their lumens. Some of the nodules had central necrosis The epitheliod cells and vascular structures were positive with CD31, factor VIII, and negative with TTF1.
Conclusion: There are many pulmonary diseases presenting with multiple nodular lesions and, EHE should be kept in mind for differential diagnosis.

PS-05-026
Histological, immunohistochemical and molecular subtyping of non-small cell lung cancer
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Objective: Recent advances have led to increasing use of targeted therapies for non-small cell lung cancer (NSCLC); the precise classification of this heterogeneous disease therefore has important clinical implications. The objective of this study was to reassess our centre's recent performance in NSCLC classification following earlier participation in the seminal LungPath study (data from 2011 to 12).
Method: All new NSCLC cases diagnosed at Queen Elizabeth Hospital Birmingham in 2013–15 were retrospectively identified (n = 566). The diagnostic frequency of individual NSCLC subtypes was determined. A subset of cases (n = 55) was randomly selected for more detailed analysis.
Results: >80 % of cases were diagnosed as either adenocarcinoma or squamous cell carcinoma. The diagnostic rate of NSCLC-NOS (not otherwise specified) was low at 4.8 % and represented an improvement of 1.3 % compared to our performance in the LungPath study. Immunohistochemistry was performed in 53/55 selected cases with a mean of 8 immunostains per case. Additionally, 48/55 cases were tested for EGFR mutations (85 % success rate) and 33/55 cases for ALK translocations (100 % success rate).
Conclusion: The low rate of NSCLC-NOS diagnosed at our centre likely results from regular use of immunohistochemistry, which particularly aids diagnosis when the primary site is unknown, and does not appear to impact on subsequent molecular testing.

PS-05-027
Pulmonary lesions with bone marrow, bone trabeculae and calcium deposition: Possible involvement of bone marrow mesenchymal stem cells in repair of lung tissue in pathological conditions
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Objective: to study morphology and molecular mechanisms of development of pulmonary lesions with bone marrow, bone trabeculae and calcium deposition.
Method: surgical material from patients with healed foci of primary tuberculosis (4 patients) and nontuberculosis mycobacteriosis (1 patient) and autopsy case of patient with candidiasis after chemotherapy and colon cancer progression (1 case). Imunnohistochemistry (IHC) analysis of Apo-Cas, Ki67, SMA, Desmin, Vimentin, CD3,20,45,68, EMA, TGF-β, CD34, PDGF, OCT-4, CD117 was done.
Results: Healed foci of primary tuberculosis were solitary and localized in 3, 6 and 7 segments of the lungs, characterized by dystrophic calcification of central caseous necrosis surrounded by fibrous capsule around with foci of bone trabeculae and bone marrow. In other patient with diffuse pulmonary osteodystrophy lesions were multiple and characherized by formation of bones with bone marrow and calcification. IHC of these lesions showed stem cells with expression of Ki67, SMA, Desmin, Vimentin, CD3,20,45,68, EMA, TGF-β, CD34, PDGF, OCT-4, CD 117.
Conclusion: Lesions with bone marrow, bone trabeculae and presence of stem cells may prove the involvement of bone marrow mesenchimal stem cells in repair of lung tissue in pathological conditions.

PS-05-028
Pulmonary carcinomas PD-L1 immunoexpression in lab routine
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Objective: PD-L1 – Programmed Death Ligand 1 – tumoural cells overexpression is understood as facilitator for tumour growth and metastasis prone for targeted therapy in nearly 50 % of pulmonary carcinomas.
Method: The 22C3 DAKO antibody was applied trough Bond Max® and Ventana Ultra® autostainers, at 1:100 dilution, following manufacturers recommended procedures after placenta/macrophages positive controls aferition.
Results: The 138 Lab positive cases immunostained for PD-L1 corresponded to BondMax® 7/24 and Ventana Ultra® 58/114, scored trough the following cut-off: + < 5 %; ++ 5–50 % and +++ > 50 %, to encompass the recognized therapy prescription. This series concerned Adenocarcinomas 22-Bond/ 70-Ventana and Epidermoid carcinomas 1-Bond/ 19-Ventana (occasional cases of Pleomorphic (+++), Large Cell (+++) and Adenosquamous Carcinomas (++) were also immunostained).
Conclusion: The positive controls (placenta and also macrophages internal positive control) were consistently applied in all runs of both immunostainers (the studies cases were not immunostained twice). The referred positive cells immunoscore was applied consistently in all cases and positive intensity was also consistent either as complete or incomplete cellular cytoplasmatic membrane immunostaining. We then advise both immunostainers for 22C3 DAKO antibody use for anti-PD-L1 therapy prescription (VA 2016; 468: 511–525 recommendations can also be added).

PS-05-029
Is idiopathic pulmonary fibrosis actually idiopathic?
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Objective: Idiopathic Pulmonary Fibrosis (IPF) is a progressive chronic interstitial pneumonia of unknown etiology with poor prognosis. We analyzed explanted lungs with a clinico-radiological diagnosis of IPF, to identify those with a specific etiology.
Method: We revised 40 explanted lungs of 40 patients with an IPF diagnosis, following clinical and radiological criteria, transplanted between the years 2011 and 2016.
Results: All cases showed a morphological pattern of Usual Interstitial Pneumonia (UIP). In 29 cases (72.5 %), a cause for lung fibrosis was found: 14 cases (35 %) showed histologic changes suggestive of Interstitial Pneumonia with Autoimmune Features (IPAF), 14 cases (35 %) showed signs of hypersensitivity pneumonitis and one case (2.5 %) was diagnosed as asbestosis.
Conclusion: IPF diagnosis is based on the clinical exclusion of known causes of interstitial lung disease, a UIP radiologic pattern by CT-scan and/or a histology with UIP pattern without other signs of an alternative diagnosis. The actual guidelines do not include the biopsy as a necessary diagnostic criterion of IFP. However, in our series, 72.5 % of patients showed histologic data of an alternative etiologic diagnosis. These results demonstrate the important role of the biopsy in the diagnostic process of this entity.

PS-05-031

Medullary thyroid carcinoma metastasis mimicking pulmonary neuroendocrine cell hyperplasia

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Objective: Pulmonary neuroendocrine cell hyperplasia (PNECH) is one of the rare preinvasive epithelial lesions of the lungs with reactive or idiopathic occurrence. We present here an interesting case of medullary thyroid carcinoma metastasis that shows the same morphological manifestation

Method: The case was that of a 74-year-old lady. She presented complaining about cough and shortness of breath. Ground glass opacity, reticulation and interlobar septal thickening were found in her high resolution thoracic tomography. With an initial diagnosis of interstitial lung disease, a surgical biopsy was performed.

Results: Emphysema and distal airway mucosa in the background of chronic bronchiolitis with surrounding cell proliferation of neuroendocrine character in the form of small cell nests were found in the pathological examination. This proliferation was in a very limited area in the parenchyma. Synaptophysin, chromogranin and calcitonin showed positive reaction. The findings were consistent with pulmonary neuroendocrine cell hyperplasia and medullary thyroid carcinoma metastasis mimicking tumours. In the thyroid gallium scintigraphy, a medullary carcinoma spot was found in the right medullary thyroid lobe.

Conclusion: The medullary thyroid carcinoma metastasis in our patient, who presented with pulmonary findings, was mimicking PNECH and tumourlet. Although encountered very rarely, it should be considered in differential diagnosis

PS-05-032

PD-L1 and CD8 expression in early stages NSCLC

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Objective: Establish the prevalence and significance of PD-L1 and CD8 expression in surgically treated NSCLC patients.

Method: We included 162 patients with stages I and II (pN0) NSCLC with follow-up. None had received chemotherapy. Immunohistochemistry for PD-L1 (22C3 pharmDx) and CD8 was performed. PD-L1 was semiquantitatively scored in tumour cells (TC). Intratumoural (TILs) and stromal (TSs) lymphocytes were estimated with CD8. Results were correlated with clinical and pathological information (chi square and Fisher tests). Overall survival (OS) and disease-free survival (DFS) estimates were determined from Kaplan-Meier analysis and compared using the log-rank test.

Results: Positive immunostaining for PD-L1 was observed in 26.5 % cases (cut-off ≥5 %). TILs were "high" (>4/100) in 28 % and TSs "high" (>59/HPF) in 50 %. PD-L1 expression was associated with younger age, high nuclear grade, high Ki67 and low TILs. We didn't find an association between other variables, including TSs. There was no significant difference in the numbers of PDL-1+ cells according to other variables, including TSs lymphocytes. PD-L1 expression showed a significant association with shorter DFS (82 versus 121 months; HR 1,95; IC 95 % 1,12-3,42; p = 0,019) and a trend for shorter OS in cases with low numbers of TILs (92 versus 110 months, p = 0,26).

Conclusion: In early stages NSCLC without lymph node involvement, PD-L1 expression in TC is associated with low numbers of TILs and morphological variables related to tumour aggressiveness. Its overexpression is an adverse factor that predicts recurrence in patients with pulmonary carcinomas.

PS-05-033

Primary melanoma of the lung: A case report

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Objective: Primary melanoma of the lung is extremely rare, accounting for 0.01 % of all primary pulmonary tumours. We present a case of melanoma of unknown primary in a 60-year old patient, presenting with multiple pulmonary nodules.

Method: An intraoperative frozen section was performed with a diagnosis of poorly differentiated malignancy, followed by left pneumonectomy, mediastinal and hilar lymph node dissection. On gross examination a well-defined tan-white solitary tumour was found in the hilar region. Two separate smaller tumours, with similar features, were identified in the upper and lower lobe.

Results: Microscopically all the tumours were composed of epithelioid focally pleomorphic cells with nested, diffuse or perivascular arrangement. Tumour cells infiltrating the bronchial epithelium in a pagetoid fashion were observed. Immunohistochemically expression of S-100, Melan-A, MITF, tyrosinase, SOX-10, Vimentin and coexpression of CEA was observed, with preservation of INI1 immunoreactivity. All the other markers were negative. Interlobar and separately dissected regional lymph nodes were uninvolved. No melanin pigment was identified (Fontana Masson stain).

Conclusion: The diagnosis of a primary pulmonary malignant melanoma is based on clinical, radiological, and pathological criteria. In our case no previous or synchronous extrapulmonary melanoma was found. Multiple nodules of the lung in the present case could be considererd intrapulmonary metastases.

PS-05-034

Diagnostic value of microRNAs derived exosomes from bronchoalveolar lavage fluid in early stage lung adenocarcinoma: A pilot study

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Objective: Exosomes contain a diverse array of biomolecules that closely reflect the biologic state of cell and tissue from which they are released. We performed this pilot study to investigate diagnostic values in bronchoalveolar lavage (BAL) fluid exosomal micro (mi)RNA in early stage lung adenocarcinoma.

Method: We chose candidate miRNAs (miR-7, miR-21, miR-126, Let-7a, miR-17, and miR-19) known as having a diagnostic value of lung adenocarcinoma. Exosomes were isolated from BAL fluid from control subjects (n = 15) and patients with lung adenocarcinoma (n = 13). Results were validated with quantitative RT-PCR.

Results: The presence of miRNAs was confirmed in exosomes from BAL fluid of both lung adenocarcinoma patients and control subjects. MiR-126 ($p < 0.001$) and Let-7a ($p = 0.015$) were present in significantly higher levels in the BAL fluid of lung adenocarcinoma patients than in control subjects. The BAL fluid miRNA signature was confirmed using an independent set of paired adenocarcinoma and normal tissue samples (n = 4). Lung adenocarcinoma tissues showed increased expression of miR-126 ($p = 0.039$) as compared to normal tissue samples.

Conclusion: BAL fluid exosomal miRNAs obtained by noninvasive methods could serve as diagnostic biomarkers in early stage lung adenocarcinoma.

PS-05-035

Higher PD-L1 expressions were associated with NSCLC patients with brain metastases

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Objective: The role of PD-L1 in lung cancer, especially those at high stage and subsets with metastasis has not been well characterized. In this study we correlated the PD-L1 expression in NSCLC and other clinicopathologic characteristics.
Method: A tissue microarray (TMA) was made from archived NSCLC samples. Immunohistochemistry (IHC) was performed for PD-L1 (SP142), p53 (DO-7), and mesothelin (5B2). Hazard ratio (HR) and 95 % confidence interval (CI) as well as survival analyses assessed the association between PD-L1 and brain metastases and overall survival (OS).
Results: In total 124 cases, majority of the tumours (74.1 %, 92/124) showed no expression (0–1). 26.7 % of tumour cells had moderate (2+) to strong (3+) membrane expressions. Brain metastatic tumours had significantly higher PD-L1 expression (55.9 %) than other patients (44.1 %) ($P = 0.002$). Meanwhile, the expression of PD-L1 is positively correlated with EZH2 ($P < 0.001$), TP53 ($P = 0.003$) but not with mesothelin ($P = 0.7919$), respectively. ANOVA analysis demonstrated that PD-L1 overexpression was not associated with KRAS or EGFR mutations. Finally Kaplan-Meier survival analyses revealed no correlation of PD-L1 expression with overall survival ($P = 0.91$).
Conclusion: In summary, we demonstrated relatively homogenous expression of PD-L1 detectable by IHC on NSCLC tumour cells. The expression of PD-L1 may be served as a potential independent predictive biomarker for brain metastasis and anti-PD-1 therapy in this subset of patients.

PS-05-037

Smoking-related interstitial lung disease: Pathologic diagnostic correlation with radiologic findings in surgical specimens

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Objective: Smoking-related interstitial lung disease comprises diverse morphological entities, including respiratory bronchiolitis (RB), desquamative interstitial pneumonia (DIP), and more recently described, smoking-related interstitial fibrosis (RB with fibrosis/SRIF). Here, we report the morphological changes encountered in a series of lung surgical specimens and the associated findings in high resolution computed tomography (HRCT).
Method: 51 specimens included from patients who had undergone lobectomy or pneumonectomy for lung cancer. After formalin insufflation, 3 to 6 sections were obtained from non-tumoural areas. RB, DIP and RBF/SRIF were semiquantitave calculated. Histopathological findings were correlated with smoking history: never smoker (NS), former (FS), light (LS, 10–34 pack-year) and heavy (HS, ≥35 pack-year) and with the findings in the HRCT.
Results: Forty-one percent of patients were HS, 12 % LS, 31 % FS and 16 % NS. RB was seen in 65 % of patients: 90 % of HS, 67 % of LS, 50 % of FS and 25 % of NS ($p = 0{,}006$); in 26/33 patients (79 %) there was HRCT evidence of RB ($p = 0.000$). DIP-like findings were seen in 63 % of patients: 95 % HS, 67 % LS, 38 % FS and 16 % NS ($p = 0.000$); 6/32 patients (19 %) exhibited HRCT findings of DIP ($p = 0.044$). RBF/SRIF was seen in 29 % of patients: 43 % were HS, 50 % LS, 18 % FS and 0 of NS ($p = 0{,}06$); in 3/15 patients there was HRCT evidence of RBF/SRIF ($p = 0{,}037$).
Conclusion: In smokers there is a high prevalence of RB, DIP and RBF/SRIF. These spectrum of changes correlate with smoking history and with HRCT findings.

PS-05-038

Primary signet ring adenocarcinoma of the lung accompanying necrotising type sarcoidosis; a case report

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Objective: Lung cancer is the most frequent and fatal cancer in the world. Subtyping of the tumour has to be done correctly in order to determine the exact treatment. Also the accompanying histopathological findings have to be evaluated carefully in order not to miss the main diagnosis.
Method: A 65-year-old female suffering from cough had a Sarcoidosis diagnosis with a small lung biopsy 2 years ago in another hospital and her cough was healed with medical treatment. However her cough have started 2 weeks ago again. On her thoracic computed tomography she had multiple masses larger of which was 5 cm in diameter in bilateral lungs and multiple lymphadenopathies in mediastinum, pulmonary hilum.
Results: Lung wedge biopsy revealed large necrosis and many granulomas with Schaumann bodies and tumour cell groups most of which were signet-ring-cells containing Alcian-Blue positive mucin. These tumour cells were stained positive with Thyroid-Transcription-Factor1(TTF-1), Cytokeratin7, Anaplastic-Lymphoma-Kinase(ALK) and stained negative with CD68, CDX2, CK20, Vimentin, Leukocyte-common-antigen(CD45).
Conclusion: The disease was diagnosed as 'Signet-ring-cell variant of Primary Lung Adenocarcinoma accompanying with and masked by Necrotysing type sarcoidosis'. This case shows that chronic benign diseases have to be followed-up carefully in order not to miss accompanying more serious diseases.

PS-05-039

Clinicopathologic values of PD-L1 expression and polymorphism in NSCLC

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Objective: PD-L1 expression has been indicated in identifying non-small cell lung carcinoma (NSCLC) patients for treatment of anti-PD-1 or anti-PD-L1 therapy, but there have been few polymorphism in PD-L1 described. The goal of this study was to evaluate the clinicopathologic values of PD-L1 expression and polymorphism in NSCLC.
Method: The 99 NSCLC tissues consisted of 50 samples of squamous cell carcinoma (SqCC) and 49 samples of adenocarcinoma (ADC). All tissue microarray paraffin blocks were used for PD-L1 IHC 22C3 pharmDx Assay (Code SK006; Dako, Glostrup, Denmark). Three single nucleotide polymorphisms (SNPs) in PD-L1 gene, rs4143815, rs822336, and rs822337 from NCBI database (http://www.ncbi.nlm.nih.gov/SNP), were genotyped using SNP pyrosequencing. Associations of PD-L1 expression and polymorphism with clinicopathologic parameters were analyzed.
Results: Ten of 49 ADC cases (25.6 %) and 29 of 50 SqCC cases (50.7 %) were positive for PD-L1 expression ($p < 0.001$). Statistical correlations between PD-L1 expression and shorter disease-free survival was found ($p = 0.028$). Statistical correlations between PD-L1 expression and shorter disease-free survival in the ADC patienets was found ($p = 0.005$). Among the 3 SNPs, rs4143815C>G was associated with short overall survival in the ADC patients ($p = 0.041$).

Conclusion: There was a significantly higher PD-L1 expression in SqCC than in ADC. But PD-L1 expression and polymorphism might be useful for the prediction of prognosis in ADC patients.

PS-05-040

E-cadherin expression in primary non-small cell lung carcinomas in relation to lymph node metastasis

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Objective: To evaluate E-cadherin expression in association with lymph node metastasis in primary non-small cell lung carcinomas (NSCLC).
Method: The retrospective study included 58 consecutive patients who underwent radical pulmonary surgery due to primary NSCLC. Staging was performed in accordance to TNM lung tumour classification by World Health Organization, 2015 (Travis et al., 2015). E-cadherin expression was detected by immunohistochemistry and evaluated as positive versus negative using cut-off level at 10 % of positive tumour cells (Deeb et al., 2004). The statistical analysis comprised descriptive statistics including calculation of 95 % confidence interval (CI), and Mann-Whitney test.
Results: The study group comprised 58 primary NSCLC cases. Lymph node metastases were found in 27 (46.6 %; CI = 34.3–59.2) patients of which 25 (92.9 %; CI = 77.4–98.0) were assessed as E-cadherin-positive and 2 (7.1 %; CI = 2.0–22.6) as negative cases. The remaining 31 (53.4 %; CI = 40.8–65.7) cases included pN0 carcinomas. Among these, 23 (74.2 %, CI = 56.8–86.3) tumours were E-cadherin-positive while 8 (25.8 %, CI = 13.7–43.2) cases were negative compared to metastatic cancers ($p = 0.058$).
Conclusion: There was a trend to more frequent E-cadherin expression in NSCLC showing metastatic spread to lymph nodes in contrast to non-metastatic tumours. The controversies regarding E-cadherin in lung cancer might be attributable to case selection, e.g., including only resectable tumours; or mesenchymal-epithelial transformation.

PS-05-041

Is papillary pulmonary adenocarcinoma a homogeneous subtype?

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Objective: One of the basic patterns in pulmonary adenocarcinoma is the papillary subtype. However, adenocarcinoma may involve papillary formations differing from each other. Our purpose here is to explore the presence of histopathological subtypes of the papillary pattern.
Method: We reviewed the resection cases where an anatomic surgical tumour operation was administered.In re-evaluation, pseudolepidic ones were classified as pattern 1, those medium sized thyroid papillary carcinoma resembling papillary carcinoma as pattern 2, and those forming large complex structures like serous ovarian carcinoma as pattern 3. Additionally, micropapillary patterns, tumour spread through air spaces (STAS), secondary dominant patterns, nuclear grades, mitoses, necroses, and vascular invasions were reviewed.
Results: A total of 41 cases were found. Their histological subtype distribution was 6 (14,6 %) papillary type 1, 24 (58,5 %) papillary type 2, and 11(26,8) papillary type 3. Unlike the other two subtypes, the pseudolepidic papillary pattern involves less micropapillary formations and STAS.Necrosis and vascular invasion were found more in papillary types 2 and 3.
Conclusion: The papillary pattern of lung adenocarcinoma does not exhibit a single uniform morphology. This result may be associated with other minor histopathological factors. This study should be analyzed on broader case series.

PS-05-042

Identification of recurrence-associated MicroRNAs in stage I lung adenocarcinoma

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Objective: Lung cancer is the most common cause of cancer-associated death worldwide. Postoperative relapse and subsequent metastasis result in high rate of mortalities in lung cancer. MicroRNAs are small non-coding RNAs that regulate gene expression at post-transcriptional level, and frequently dysregulated in various cancers. The aim of this study was to identify recurrence-associated microRNAs in early stage of lung cancer.
Method: To screening the differentially expressed microRNAs related to postoperative recurrence, microRNA microarray data derived from stage I lung adenocarcinoma formalin-fixed paraffin embedded (FFPE) tissue samples ($n = 6$) and publically available The Cancer Genome Atlas (TCGA) data was analyzed. Independent sample ($n = 30$) was used for validating the candidate microRNAs by real-time polymerase chain reaction (RT-PCR).
Results: In microRNA expression profiling data, we identified 60 significantly dysregulated microRNAs in relapsed stage I adenocarcinoma. Using TCGA cohort, 24 dysregulated microRNAs were found. Three microRNAs (let-7 g-5p, miR-143-3p, and miR-374a-5p) were associated with postoperative recurrence in both datasets. All three candidate microRNAs were validated in the independent cohort of stage I adenocarcinoma by RT-PCR.
Conclusion: We discovered three recurrence-associated microRNAs of early lung adenocarcinoma using FFPE tissue, which showed possible clinical utility as a biomarker predicting recurrence. Further investigation for functional properties of these microRNAs in lung adenocarcinoma is needed.

PS-05-043

Differential microRNA expression of EGFR T790M mutated and tyrosine kinase inhibitor-sensitive EGFR mutated lung cancer

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Objective: MicroRNAs (miRNAs) are short, non-coding RNAs that mediate post-transcriptional gene regulation and they are commonly deregulated in human malignancies including non-small cell lung cancer (NSCLC). The aim of this study is to investigate the expression of miRNAs in epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs) resistant T790M-mutated NSCLC.
Method: We performed miRNA PCR array profiling using 4 cases of EGFR T790M-mutated NSCLC and 5 cases of L858R-mutated NSCLC. After identification of differentially expressed miRNAs between two groups, they were validated by quantitative real-time reverse transcription polymerase chain reaction (qRT-PCR), using 6 cases of resected NSCLC harboring T790M mutation.
Results: We identified 3 up-regulated miRNAs whose expression levels were altered by 4.0-fold or more in EGFR T790M mutation group compared to L858R group by miRNA PCR array profiling and they are miR-1 (fold change 4.384), miR-196a (fold change 4.138), miR-124 (fold change 4.132). The differentially expressed 3 miRNAs were validated by qRT-PCR and they were over-expressed in T790M group relative to L858R group. Especially, miR-1 and miR-124 showed significantly higher expression levels in T790M group (p-value of miR-1 = 0.0004277, miR-124 = 0.001654, miR-196a = 0.05057).

Conclusion: MiR-1, miR-124 and miR-196a were over-expressed in EGFR T790M mutated NSCLC.

PS-05-045

Histologic evaluation of tumour infiltrating lymphocytes (TILs) with H&E section in primary lung adenocarcinoma: A practical method for prognostic prediction

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Objective: Prognostic significance of tumour-infiltrating lymphocytes (TILs) has been determined in cancers of lung, colon and breast. Although there is a consensus for measurement of TILs in breast and colon cancers, there is no standardized method for lung cancer. Here, we applied modified version of immunoscoring for breast cancer to lung adenocarcinoma.
Method: A cohort of 146 lung adenocarcinoma patients who underwent lobectomy with lymph node dissection were included. The full face sections of H&E slides were reviewed. We evaluated TILs level as a percentage of area occupied over total intratumoural stromal area. Peribronchial areas were excluded. Histopathologic factors include histologic grade, necrosis, extracellular mucin, lymphovascular invasion, lymph node metastasis, TIL level, tertiary lymphoid structures (TLSs) around tumour and presence of germinal center (GC) in TLSs.
Results: The high level of TILs was significantly correlated with differentiation ($p = 0.023$), necrosis ($p = 0.042$), abundance of TLSs ($p < 0.001$) and presence of GC in TLSs ($p = 0.004$). High level of TILs was associated with better progression-free survival ($p = 0.017$) and overall survival ($p = 0.049$).
Conclusion: Modified version of measurement for TIL level in breast cancer has a high reproducibility. Histologic evaluation of TILs level in lung adenocarcinoma with the same method has a prognostic value in routine surgical pathology.

PS-05-046

Clinico-pathological and molecular characteristics of patients with NSCLC

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Objective: Determination of the clinico-pathological and molecular characteristics of patients with NSCLC.
Method: This retrospective, descriptive and analytical study involved 350 patients with NSCLC recruited in CHU Hassan II, Fes, during 63 mounth extending from 01/01/2011 to 01/03/2016. Data information and molecular abnormalities were obtained from the pathological and clinical records of patients.
Results: The average age of patients was 59 years. Among 350 patients, 80 % were male. The most common clinical presentation was pain (75 %) followed by hemoptysis (30 %). Thoracic CT was performed in all patients, tumour size were classified as T1 (4 %), T2 (25 %), T3 (17 %) and T4 (54 %). 94 % of patients had metastases at the time of diagnosis. Pulmonary adenocarcinoma was the most frequent histologic type (75 %) followed by squamous cell carcinomas (22 %), whereas large cell neuroendocrine carcinomas were only 3 %. The expression of CK7, TTF1, CK5 / 6, P63 and synaptophysin was statistically significant ($p < 0.00001$). In our series the mean survival of our patients was estimated to be 280 days, significantly increased in subjects <50 years (345 days) ($p = 0.027$). A molecular study of EGFR was performed in 15 patients, that two of them showed a deletion at exon 19 of the EGFR gene.
Conclusion: This type of cancer is very common in our region. Metastatic stages were the most observed. This study will be supplemented by a thorough genetic study in order to establish correlations between the mutational profiles and clinical-pathological parameters in order to improve the management of the patients.

PS-05-047

Pulmonary alveolar microlithiasis. A case report with review of literature

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Objective: Pulmonary alveolar microlithiasis (PAM), is a rare and diffuse lung disease, around 800 cases have been reported in the literature to date. It is characterized by intra-alveolar accumulation of lamellar calcium deposits in bilateral lung parenchyma. Here we report a case of this infrequent disease.
Method: A 43-years-old man presented with dyspnea. Subsequent chest high-resolution Computed Tomography (HRCT) revealed a fine, sandlike micronodular pattern. Patient was given symptomatic treatment and was referred to our centre for lung transplantation. Single lung transplantation was performed.
Results: The surgical specimen was enlarged and heavy, measured 18 × 17 × 8 cm and weighted 1500 g. Histologically, the pulmonary architecture was diffusely altered because of the filling of alveoli with multiple microliths. Patchy inflammation was frequently present with variable degrees of interstitial fibrosis as well as osseous metaplasia.
Conclusion: PAM has been considered to be an autosomal recesive disorder because it is transmits horizontally and is associated with consanguinity. The clinical course is not uniform. The optimal diagnostic procedure is the association of chest HRCT with bronchoalveolar lavage. The differential diagnosis may include miliary tuberculosis and sarcoidosis. At present lung transplantation is the only effective therapy. However, better knowledge of the gene responsible offers hope for new therapies.

PS-05-048

Primary pleural epithelioid hemangioendothelioma: A case report and review of literature

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Objective: Epithelioid hemangioendothelioma (EHE) is a rare vascular tumour. It commonly affects liver, lung and bones. Pleural involvement is extremely rare with less than 30 cases reported in the literature. We aim to describe another case primary EHE of the pleura with a review of literature.
Method: A 79-year-old man with history of chronic obstructive pulmonary disease presented with right-sided chest pain and breathlessness. On physical examination there was dullness to percussion and decreased breath sounds over the right hemithorax with signs of heart failure. Computerized tomography revealed multifocal right pleural thickening and effusion. A pleural biopsy was performed.Chest radiograph confirmed the presence of pleural effusion. Computerized tomography (CT) revealed multifocal right pleural thickening and effusion. Image-guided pleural biopsy was performed.
Results: Microscopically, the tumour showed a biphasic pattern with cords and nests of epithelioid cells set in a myxoid stroma. Some cells show mild atypia and rare mitosis with intracytoplasmic lumina containing red blood cells. The second pattern is composed of spindle-shaped cells with occasional necrosis. Immunohistochemically, the tumour cells were positive for CD34 and focally with CK7. The diagnosis of EHE with high grade pattern was made. Unfortunately, the patient passed away 1 month later.

Conclusion: Considering its rarity and its aggressive behavior, it is important we continue to collect data in order to establish clinical and prognostic profile of this tumour.

Monday, 4 September 2017, 09:30–10:30, Hall 3
PS-06 Dermatopathology

PS-06-001
Follicular involvement in malignant melanoma
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Objective: In the last decade, following the reporting of follicular melanoma as a distinct entity, the issue of involvement of hair follicle with melanoma cells attracted attention. We aimed to review cases from our archives to evaluate follicular involvement by melanoma, analyze infiltration patterns according to recently proposed classification system.
Method: Excisional biopsies of all melanoma cases diagnosed between 2006 and 2016 were reviewed.
Results: Ninety two cases of melanoma were reevaluated (75 cases of invasive melanoma(81,6 %), 17 cases of melanoma in situ (18,4 %)) and follicular involvement was seen in 50 % of cases. The cases showed no apparent sex predilection and most of them were localized at head and neck region (71,7 %). Most of the cases presented with involvement limited to infundibulum of hair follicle (41,3 %). In 10 cases, destruction of hair follicle by melanoma cells was also noted.
Conclusion: Involvement of hair follicle is a finding observed not infrequently in melanoma cases. Lack of recommendations in current guidelines causes it to be neglected at standard reporting. To determine its possible associations with prognosis, a need to revise guidelines to include this finding seems to be a necessity.

PS-06-002
Two cases of primary cutaneous Ewing sarcoma/primitive neuroectodermal tumour confirmed by molecular methods: S100 protein positivity can be a pitfall
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Objective: Primary cutaneous Ewing sarcoma/primitive neuroectodermal tumour (ES/PNET) is a rare malignant small round-cell tumour. Here we present two cases with immunohistochemical and molecular findings.
Method: Florescence in situ hybridization (FISH) analysis using dual-color break-apart probe for EWSR1 gene and reverse-transcriptase polymerase chain reaction (RT-PCR) for EWSR1-FLI1 fusion gene were performed.
Results: Two patients presented with small solitary tumours on the skin: A 25-year-old female with an acneiform lesion on the cheek and a 7-year-old male with a nodule on the knee. An infiltration of small round-cells in the dermis and subcutaneous fat was seen. Tumour cells showed immunoreactivity for CD99, caveolin-1 and S100 protein. Other small round-cell tumours in the differential diagnosis were excluded using broad immunohistochemical panel. FISH analysis revealed EWSR1 gene rearrangement and RT-PCR analysis showed type 1 fusion product between EWSR1 exon 7 and FLI-1 exon 6 generated by t(11;22)(q24;q12).
Conclusion: Despite the low frequency, ES/PNET should be kept in mind in the differential diagnosis of small round-cell tumours of the skin. CD99, caveolin-1 and FLI-1 are well-known immunohistochemical markers. However, one should also be aware of the possible S100 protein expression in ES/PNET to prevent misdiagnosis. Although immunohistochemistry is helpful, molecular analysis is a requisite for the definitive diagnosis.

PS-06-005
Lymphomatoid papulosis - a case report of a special localisation
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Objective: Lymphomatoid papulosis(LP) is a subtype of the CD30-positive T-cell lymphomas with cutaneous manifestation (CTLT). Currently, it is considered a low-grade CTLT, its uniqueness being given by the discrepancy between the histological features, suggesting a highly malignant status, and the clinical self limiting proprieties of the relapsing chronic lesions.
Method: We present the case of a 43-year-old male, with a history of chronic reoccurring dark red / brown papulous lesions located strictly at the ear-lobe level, bilateral.
Results: The microscopy images are dominated by rich dermal infiltrate of lymphoid cells, containing large, regular or irregular nuclei, with eosinophilic nucleoli and rich cytoplasm ;frequent atypical mitosis are also present, suggesting the malignant aspect, over a hyperkeratotic epidermis background. Using immunohistochemistry, we find that the large, atypical lymphocites presented themselves as CD3+, CD5+, CD10-, CD15- and CD30+, while the rest of the small lymphoid cells were CD20 marginally positive. We consider this case as a LP one. Given the histopathologycal results, the patient was treated with local liquid nitrogen application, achieving partial remission.
Conclusion: We believe the particularity of this case is given by the unique localisation of the lesions, since this is the first documented case located solely in the described areas.

PS-06-006
Cutaneous clear cell sarcoma with intraepidermal component mimicking spitzoid melanoma
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Objective: To report a case of cutaneous clear cell sarcoma (CCCS) with intraepidermal component mimicking spitzoid melanoma and to discuss the diagnostic approach.
Method: 20-year-old male presented with a nodular lesion on the dorsum of the foot that was marginally excised. We examined the lesion by light microscopy, immunohistochemistry and FISH analysis.
Results: Histopathological examination revealed poorly circumscribed tumour centered in the dermis with several nests in the overlaying epidermis and focal extension into the superficial subcutis. Tumour cells were mostly elongated with moderately pleomorphic vesicular nuclei and abundant lightly eosinophilic cytoplasm, organized in an fascicular, nested and focally discohaesive manner. Numerous »wreath like« giant cells were apparent among the lesional cells. By immunohistochemistry, tumour cells were positive for S100, melanA and HMB45. FISH analysis using a break-apart probe for EWSR1 detected rearrangements in 79 % of the tumour cells.
Conclusion: Intraepidermal colonization by CCCS is extremely rare event reported only twice. Since distinctive morphological features of CCCS can be lacking, compound variant further causes diagnostic challenges due to morphological and immunohistochemical overlap with melanocytic lesions. Molecular assessment is crucial since the chromosomal translocation t(12;22) resulting in EWSR1-ATF1 fusion is the hallmark of CCS and has not yet been reported in melanoma.

PS-06-007

Spitzoid neoplasms: Clinical and histopathological features in correlation with ALK immunoreactivity

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Objective: Spitzoid melanocytic tumours are a clinical, histopathological and molecular heterogenous group of skin tumours. Translocation of the anaplastic lymphoma kinase(ALK) have been found in spitzoid neoplasms leading to kinase fusion proteins that can be detected immunohistochemically.
Method: Here we described the clinical and histopathological features of 33 Spitz tumours(19 Spitz nevi(SN), 11 atypical Spitz tumours(AST) and 3 spitzoid melanomas(SM)) and correlate them with the immunoreactivity for ALK.
Results: We found ALK positivity in 54 % of ATS, in 32 % of SN and in 0 % of SM included in the study. The majority of ALK positive tumours were diagnosed in females(71,57 %), aged between 8 and 55 years, and were located in trunk region(45,54 %); 27, 62 % of the ALK positive tumours were identified in paediatric patients. Plexiform tumours displayed ALK positivity. There was a tendency toward ALK-positive tumours being hypo-/amelanotic. A halo reactions was observed in 27,27 % of the spitzoid tumours with ALK immunoreactivity.
Conclusion: Morphologic appearance of the lesion is linked to the ALK expression and thus to molecular changes. There was no relation between ALK positivity and malignancy, but the results aren't statistically significant(too few cases of SM). In our study, there was a tendency towards developping ALK-positive spitzoid tumours in female patients.

PS-06-008

Ex-vivo dermoscopy as an aid in dermatopathology practice: A pilot study

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Objective: The purpose of the study was to evaluate if ex-vivo dermoscopy could be useful in gross examination of skin biopsies.
Method: On gross examination 143 ex-vivo skin lesions were evaluated by senior dermatopathologist, fellow, one senior and two junior residents, as well as by dermoscopy (by the same senior resident). The concordance of macroscopic/dermoscopic and histopathological diagnoses was examined using kappa statistics.
Results: Dermoscopy showed almost perfect agreement with histopathology in diagnosing tumours of epidermal origin ($p<0.001$). Substantial concordance was found in overall cases, as well as in benign and malignant tumours, in situ/dysplastic lesions, and tumours of melanocytic origin ($p<0.001$). This level of agreement was only met by senior dermatopathologist in gross examination of overall cases, malignant tumours and those of epidermal origin ($p<0.001$). Training in dermatopathology improved gross assessment by fellow and senior resident compared to junior residents, but with only moderate concordance in overall cases, benign, malignant and tumours of epidermal origin ($p<0.001$). No more than fair level of agreement in diagnosing in situ/dysplastic lesions was met, also by senior pathologist ($p = 0.043$).
Conclusion: Ex-vivo dermoscopy is superior in gross assesment of skin biopsies, and it could be useful tool especially in examination of melanocytic tumours and in situ/dysplastic lesions.

PS-06-009

A case of congenital dermatofibrosarcoma protuberans confirmed by florescence in situ hybridisation

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Objective: Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive mesenchymal tumour of the skin that rarely affects children. Congenital cases are extremely uncommon. We present a case of congenital DFSP with florescence in situ hybridization (FISH) findings.
Method: FISH analysis using dual-color dual fusion probe for type 1 collagen alpha 1 - platelet-derived growth factor beta (COL1A1-PDGFB) fusion gene was performed.
Results: Incisional biopsies of an irregular red plaque and satellite lesions on the left hip of an 8-month-old female existing since birth were evaluated. The clinical diagnosis was tufted hemangioma. An infiltration of spindle cells extending from the papillary dermis to the subcutaneous fat tissue in a honeycomb pattern was observed. CD34 was positive and factor XIIIa, S100 protein and smooth muscle actin were negative. COL1A1-PDGFB fusion gene generated by t(17;22)(q22;q13) was demonstrated by FISH analysis.
Conclusion: Recognition of congenital DFSP in clinical practice may be problematic due to its resemblance to vascular lesions. A skin biopsy is required for the diagnosis. Histopathologic differential diagnosis includes various spindle cell tumours. Infiltration of the fat tissue in a honeycomb pattern is a peculiar finding and CD34 immunopositivity is supportive. However, detection of the specific fusion gene by molecular methods is essential for the definitive diagnosis.

PS-06-010

Large-cell transformation of mycosis fungoides: Report of 11 cases

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Objective: Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma.A minority group of mycosis fungoides(MF) patients undergo a process of large-cell transformation(LCT), which often is characterized by an aggressive behavior. The aim of this study is to discuss the clinical, histological and immunophenotypical features and prognostic value of LCT.
Method: Eleven cases with LCT in MF diagnosed between 2000 and 2017 were studied.
Results: Patch, plaque and/or tumoural lesions were observed in the study group, including 9 males and 2 females, with median age of transformation 60.2 years-old and median time of transformation 9 years (range, 4–30 years). All skin biopsies revealed a superficial/deep dermal infiltration of atypical lymphocytes composed of >25 % large neoplastic cells. Epidermotropism was absent in two cases and very few in one, meanwhile folliculotropism was observed in five patients. Immunphenotypically CD30 was strongly positive on large neoplastic cells in four cases, weak in five, whereas two were negative. Four patients had nodal involvement. All received chemotherapy, radiotherapy and/or total body electron beam therapy. One CD30-negative case died after 1 year of LCT diagnosis.
Conclusion: Patient's early stage MF history is important in terms of differential diagnosis. Older age, advanced initial disease, short transformation period and CD30 negativity were detected as worse prognostic factors, but larger series are required to validate the prognostic significance of these features.

PS-06-011

Endocrine mucin-producing sweat gland carcinoma of the eyelid-case report and review the literature

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Objective: Endocrine mucin-producing sweat gland carcinoma (EMPSGC), is a rare adnexal tumour of the skin, which is believed to be a precursor of primary cutaneous mucinous carcinoma (PCMC)
Method: Report a case and review the literature.
Results: A 84-year-old female presented with a 6 x 4 mm lower eyelid's papule. It was a well-circumscribed dermal tumour, showing a lobular architecture with solid and cribriform patterns. The tumour cells were monomorphic. Mucin production was detected by PAS/AB. Estrogen and progesterone receptors were positive, the tumour cells were strongly and focally positive for synaptophysin and chromogranin. A rim of myoepithelial cells was evident around some tumour nodules corresponding to an in situ component. In the 56 cases reported in the literature EMPSSGC occurs more frequently in females' eyelid and presents as a solitary slow-growing skin-coloured plaque.
Conclusion: This report describes a rare eyelid's tumour. The clinical impression often suggests a benign condition namely epidermal cyst, chalazion, hidrocystoma and syringoma. Its recognition is important as it may represent a precursor of PCMC which has a more aggressive behaviour. Given its putative clinical potential the complete excision is advisable.

PS-06-012

Correlation between clinical and pathological response after neo-adjuvant electrochemotherapy in vulvar squamous cell carcinoma: A preliminary study

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Objective: Electrochemotherapy (ECT) is a potential treatment for solid tumours. In this study, we focused on pathological findings after neo-adjuvant ECT used for a local control of the disease in Vulvar Squamous Cell Carcinoma (V-SCC), analyzing the pathological regression and his correlation with the clinical response.
Method: We enrolled nine patients with histological diagnosis of primary V-SCC and eligible for surgery and ECT. Patients were reviewed after ECT and clinical response to therapy was evaluated using RECIST criteria. Surgery and pathological exams were subsequently performed with the evaluation of pathological regression.
Results: Clinical response, evaluated by RECIST criteria and pathological regression, evaluated quantifying the percentage of neoplastic volume replaced by inflammatory infiltrate and fibrosis, didn't show a linear correlation: 1 CR (with complete pathological regression), 6 PR (3 with mild pathological regression, 2 with moderate regression and one with heterogeneous regression, ranging from mild to moderate) and 2SD (one with mild regression and one with heterogeneous regression, ranging from mild to moderate).
Conclusion: This data demonstrate that ECT could be an efficacious therapeutic tool in the neo-adjuvant treatment of the V-SCC but although limited to a small series, shows that there isn't an exact correlation between clinical and pathological response, suggesting that could be useful integrate both assessments to obtain a more accurate "treatment response staging" to ECT.

PS-06-013

Jadassohn nevus - association with other tumours as problem of patient's management

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Objective: Jadassohn nevus (JN) represent a complex congenital hamartoma sometimes associated with various benign cutaneous lesions (seborrheic keratosis, basaloid hamartomas, verruca vulgaris, nevocellular nevi, adnexal tumours), intermediate malignancies (keratoachantoma, proliferating trichilemal cyst) or malignant (basal or squamous cell carcinoma, adnexal carcinomas, melanoma, leiomyosarcoma) or with oculocerebrocranial/orthopedic developmental abnormalities (sebaceous/epidermal nevi syndrome).
Method: We retrospectively reviewed 59 cases of JN diagnosed in the last 14 years in our department.
Results: Sixteen cases presented associated lesions, 4 of them being associated with multiple lesions. We identified 9 cases with associated single or multiple benign lesions (7 tricoblastomas, 4 siringomas 1 sebaceoma, 2 seborrheic keratosis and one basal cell hamartoma), one case associated with a low grad tumour (keratoacanthoma) and 6 associated with malignant lesions (4 basal cell carcinoma and two squamous cell carcinoma). None of the patients had skeletal, cerebral or ocular anomalies.
Conclusion: Identification of neoplasms associated to JN is very important considering the frequency of co-occurring malignancies in JN. Considering that most of the JN are located in the head and neck, this association can raise problems of surgical management

PS-06-014

A rare neoplasm of conjunctiva: Inverted follicular keratosis

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Objective: Inverted follicular keratozis is a uncommon solitary benign tumour and it is a variant of seborrhoeic keratosis. It occurs most commonly on the face, although on conjunctiva is infrequent.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E.
Results: We report 60 year old man patient who had conjunctival mass in the right eye. A complete excision of the lesion was performed.The histopathological analysis showed an inverted, cup shaped lesion composed of proliferations of basaloid cells and observed squamous eddies and follicular changes.
Conclusion: Viral warts, seborrhoeic keratozis and actinic keratozis should be kept in mind in differantional diagnosis. The benign lesion of inverted follicular keratozis could be distinguished from squamous cell carcinoma. Histopathologically squamous eddy formation and lack of epithelial dysplasia were significant of inverted follicular keratozis. İnverted follicular keratozis is a unusual occurring lesion found on the conjunctiva and should be included in the list of differential diagnoses of conjunctival masses.

PS-06-015

Urticarial Vasculitis - a study of 8 cases

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Objective: Urticarial vasculitis (UV) is a rare clinico-pathologic entity that is characterized histologically by leukocytoclasis, fibrinoid necrosis around small vessels and clinically by

prolonged urticarial plaques. It is aimed to describe clinical and histological features , laboratory findings, treatment of UV in patients that was evaluated in Dermatopathology Department of our hospital.
Method: Patients who applied to dermatology clinic of Okmeydanı Training and Research Hospital between 2013 and 2016 were enrolled in this study. Samples with histologic features of leukocytoclastic vasculitis were extracted from the archive and reevaluated. The laboratory, epidemyologic, clinical features and treatment outcomes were reviewed via patients files.
Results: Eight patients diagnosed as UV were assessed in this study. All patients had itchy, erythematous plaques. On histological exam , 2 patients had fibrinoid necrosis, 3 patients had leukocytoclasis and there was none of them in the other 3 patients. Immunological parameters such as C3,C4,RF,ANA,Ig E,ANCA's were examined as well as the other parameters such as hemoglobin, leukocyte, ESR and CRP. Also, direct immun florasence (DIF) method was performed on 4 patients.
Conclusion: Laboratory findings of patients with UV are variable. Clinical or histopathological findings alone are not sufficient for definitive diagnosis of UV. Clinical correlation with histopathological findings may be essential in such cases.

PS-06-016
Can amyloid patterns at salivary gland biopsies give clues for amyloidosis subtyping?
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Objective: Amyloidosis can be diagnosed by histopathological demonstration of amyloid deposits at abdominal fat biopsy or minor salivary gland as well as at involved organs. The pattern characteristics of these deposits indicating the type of amiloid protein is not clear.
Method: Patients diagnosed as amyloidosis by minor salivary gland biopsies or surgical specimens were included in this study. Sixteen minor salivary gland biopsies and two salivary gland resections were reevaluated with Kongo-red staining and digitally powered polarization technique. All cases were confirmed with the target organ biopsies.
Results: Eleven(61 %) cases were female, seven(39 %) cases were male. Amyloid deposits were classified as vascular, interstitial or mixed pattern. The association of these patterns with the amyloid etiologies was investigated. In five AL cases with myeloma, interstitial deposits were predominantly observed. Vascular and/or interstitial pattern were seen both in 11 cases with AA amyloidosis. Interstitial deposition was more by eight cases whereas three were vascular. Amyloid deposits were mixed in two cases with nor AA or AL etiology. There was no significant difference between the amyloid deposition patterns according to amyloidosis types.
Conclusion: Although minor salivary gland biopsies in this study were performed due to the Sjögren's syndrome clinic; all cases were confirmed with the target organ biopsies. The relationship between the pattern of deposits and amyloid precursor protein couldn't established. Considering the low number of our cases, we think that more studies with larger series are needed.

PS-06-017
Sclerosing melanocytic lesions (sclerosing melanomas with nevoid features and sclerosing nevi with pseudomelanomatous features): A histopathological analysis of 90 lesions
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Objective: Sclerosing melanocytic lesions, characterized by dermal sclerosis and frequently a trizonal pattern, are diagnostically challenging and remain poorly characterized. Our aim was to systematically analyze their morphologic spectrum, especially the distinction between sclerosing nevus and sclerosing melanoma.
Method: We collected prospectively 90 sclerosing melanocytic lesions, occurring in 83 patients (50 male, 33 female; age range, 21 to 89 years).
Results: A prominent pagetoid spread was identified in 44 (49 %), and a melanoma in situ adjacent to sclerosis in 55 (61 %) lesions. In the intrasclerotic component, maturation was absent in 40 (44 %) and mitotic figures were identified in 18 (20 %) lesions. Based on morphology, 26 (29 %) lesions were diagnosed as nevi, 19 (21 %) as melanomas and 45 (50 %) as melanomas with an accompanying nevus (Breslow thickness of melanomas, 0.4 to 1.8 mm; median, 0.75 mm). A 4-probe FISH assay targeting 6p25, 6q23, Cep6, and 11q13 was positive in the intrasclerotic component in 15 of 25 lesions diagnosed as melanomas and 0 of 16 lesions diagnosed as nevi. A sentinel lymph node biopsy, performed for 17 lesions, was negative in all cases.
Conclusion: Sclerosing melanocytic lesions form a morphologic spectrum and include nevi, often with pseudomelanomatous features, as well as melanomas.

PS-06-020
Lymphomatoid keratosis, a benign condition that mimics mycosis fungoides (a clinicopathological, immunohistochemical and molecular study)
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Objective: Lymphomatoid keratosis (KL) was thought to be a variant of benign lichenoid keratosis showing lymphomatoid features. Recently, it is considered as a rare variant of cutaneous lymphoid hyperplasia with epidermotropism and should be differentiated from unilesional Mycosis Fungoides (MF).
Method: We report six patients diagnosed of KL from 2010 to 2017. Clinical information of the patients was collected, including age, sex and clinical manifestations. Immunohistochemical study was performed with CD3, CD20, CD4, CD8,CD7, CD30, TCRbetaf1 and TCR gamma. Gene rearrangement of the T-cell receptor TCR-beta and TCRγ was also investigated by the polymerase chain reaction method.
Results: All the cases showed a lymphocytic infiltration in the upper dermis with epidermotropism and alignment of lymphocytes along the basal layer. The lymphoid population included CD3 cells and CD4-positive cells were predominant than CD8 –positive cells with CD2O cells intermingled. The T cells were positive for TCRbetaf1 in all the cases and TCRγ gene rearrangements were demonstrated in 2 cases.
Conclusion: LK is a benign condition with histopathological features that resemble Mycosis Fungoides. A feature which may help to distinguish LK from MF is the presence of many B cells intermingled with T cells and the presence of T and B cells with epidermotropism.

PS-06-023
Impact of insulin resistance on epidermal growth factor receptors in patients with seborrheic keratosis
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Objective: To examine epidermal growth factor receptors (EGFR) expression in patients with seborrheic keratosis (SK) and insulin resistance (type 2 diabetes mellitus) and in patients without concomitant carbohydrate metabolism disorders.
Method: The study involved 80 patients with SK, 40 of them with concomitant type 2 diabetes mellitus. The immunohistochemical test with monoclonal antibodies to EGFR (clone EGFR.25) has been performed.
Results: Intense diffuse staining of the tumour cells membranes has been identified in 32 patients with type 2 diabetes mellitus (80 %), moderate staining - in 6 patients (15 %) and weak — in 2 (5 %). A positive reaction was weak by patients without concomitant carbohydrate metabolism disorders in 28 cases (70 %), moderate - in 8 patients (20 %) and pronounced - in 4 patients (10 %).
Conclusion: EGFR overexpression identified in patients with SK and concomitant type 2 diabetes mellitus has been conditioned by insulin resistance, wherein insulin signal transmission control failures in the cell result in changes in the EGF synthesis and signaling pathway, controlling cell proliferation and growth.

PS-06-024
Which histopathological features can help the differential between clinical diagnosis of palmoplantar psoriasis and eczematous dermatitis
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Objective: Palmoplantar psoriasis and eczematous dermatitis overlap both clinically and pathologically. We examined histopathological features to identify possible clues to help this differential.
Method: Onehundredfiftyone cases, with clinical prediagnosis of psoriasis and/or eczema were searched from pathology archive. The histomorphologic features were compared with the clinical and pathological diagnosis.
Results: The features seen more common in psoriasis were; spotty parakeratosis (50 %, 20 %), polymorphonuclear leukocytes at parakeratosis (57 %, 23 %, $p < 0.001$), granular layer loss (74 %, 29 %), psoriasiform hyperplasia (93 %, 53 %, $p < 0.001$), thin rete and suprapapillary epidermal thinning (57 %, 10 %, $p < 0.001$), spongiform pustules (18 %, 3 %). The features favoring eczema over psoriasis were, hypergranulosis (35 %, 6 %, $p < 0.001$), exocytosis (64 %, 41 %, $p = 0.006$), dyskeratotic cells (37 %, 11 %, $p = 0.001$) and interstitial eosinophils (14 %, 4 %, $p = 0.047$). Presence of fibroblastic activity, vascular proliferation, extravasated erythrocytes, and dermal edema were not found to be different among groups. When clinical diagnosis were compared with pathological diagnosis; the pathological verification ratios were 60 , 32 , 100 and 60 % in the clinical diagnosis groups of psoriasis, psoriasis favoring over eczema, eczema, and eczema favoring over psoriasis.
Conclusion: For differential diagnosis of palmoplantar psoriasis and eczema, single histopathological feature does not seem to be pathognomonic, but when the whole criteria is evaluated together the diagnostic accuracy increases.

PS-06-025
Nucleoli and nuclear pseudoinclusions in cutaneous melanoma cells - a new prognostic approach to an old concept
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Objective: To assess the relationship between the cytomorphological characteristics of nucleoli and presence of nuclear pseudoinclusions and detailed clinicopathological parameters of melanoma patients.
Method: Three characteristics of cancer cell nucleoli, namely the presence, size and number, and presence of nuclear pseudoinclusions were assessed in H&E-stained slides from 96 formalin-fixed paraffin-embedded primary cutaneous melanoma tissue specimens. The results were correlated with classical clinicopathological features and patient survival.
Results: Higher prevalence and size of nucleoli were associated with thicker and mitogenic tumours. All three nucleolar characteristics were related to the presence of ulceration. Moreover, nuclear pseudoinclusions were also associated with high mitotic rate and ulceration of primary tumour. Increased prevalence and number, but not size of nucleoli were connected with shorter cancer-specific and recurrence-free survival. Furthermore, presence of nuclear pseudoinclusions was also associated with unfavorable outcome in melanoma patients.
Conclusion: (1) High representation of cancer cells with distinct nucleoli, greater size and number of nucleoli per cell and with nuclear pseudoinclusions present are characteristics of aggressive phenotype of melanoma, which may require more intensive treatment and follow-up. (2) Cytomorphology of nuclei and nucleoli should be assessed during routine review of cutaneous melanoma H&E slides as a standard, potentially informative and inexpensive procedure.

PS-06-026
Case of cutaneous protothecosis
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Objective: Protothecosis is a rare opportunistic infection caused by achlorophyllous alga Prototheca. Usually it affects dogs, cats and cattle with the development of enteritis, mastitis, and meningoencephalitis. P. Wickerhamii и P. Zopfii, responsible for the human cases of disease, are ubiquitous in nature, found especially in ponds, soil and animal waste.
Method: We had a case of skin protothecosis in 66 year old woman from Moscow region. In anamnesis there was an operated colonic adenocarcinoma with colostoma that was opened at the beginning of the disease. The patient had a contact with manure from the zoo, which she used as biological fertilizer.
Results: Skin lesions were presented by large crusted and eroded plaques, located on lower abdomen (the first manifestation), shin and forearm (appeared 10 months later). The histological examination of the deep incisional biopsy revealed pseudocarcinomatous hyperplasia of epidermis with microabscesses, containing sporangia and single lancet-like double-membrane coated organisms; diffuse dermal mixed-cell inflammatory infiltrate with multiple granulomas, composed of epithelioid and giant cells; scarring in deep dermis with multiple dead sporangia among collagen fibers.
Conclusion: Based on histological examination protothecosis of the skin was diagnosed. Combined therapy (surgical excision with itraconasole administration) was applied. 6-month follow-up showed no recurrence.

PS-06-027
Cutaneous myxofibrosarcoma in young adult: Case report
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Objective: Myxofibrosarcoma (MFS) is a relatively rare tumour that is histologically characterized by myxoid stroma and spindle cell proliferation. This tumour most commonly arises as a slow growing, enlarging painless mass in the extremities of elderly patients.
Method: We report a case of a primary, low-grade MFS in the leg of a 30-year-old man.

Results: A wide excision of a lower limb tumour measuring 10 cm in its highest diameter was performed. The gross specimen measured 10 × 4 × 4 cm, and the lesion within the specimen was semitranslucent, gelatin-like, and with foci of hemorrhage and cyctic transformation. Histologic examination showed a multicyctic lesion with a prominent myxoid matrix. A small number of irregular, spindle-shaped, or stellate cells, with hyperchromatic nuclei were noted. According to the modified FNCLCC grading system, the tumour in this cases scored 4 (tumour differentiation; score 2, mitotic count; score 1, tumour necrosis; score 1), that is, grade 2.
Conclusion: We presented a rare case of a large tumour with clinical and histopathological features of low-grade MFS in the leg. Immunohistochemistry is not of a great help for the diagnosis and only the histological examination is the clue for the final diagnosis.

PS-06-028
Pilomatricoma: Analysis of 24 paediatric cases
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Objective: Pilomatricoma(calcifying epithelioma of Malherbe) is a common skin neoplasm in the paediatric population that is often misdiagnosed as other skin conditions or tumours.The objective of the present retrospective study was to review the clinical and histopathological presentation of this neoplasm in children.
Method: The records were searched for all cases of pilomatricoma between 2011 and 2015 at pathology department,and reviewed to determine sex,age,location,size of the tumour,pathological features and recurrence rate.All patients underwent surgical excision.
Results: A total of 24 lesions in 24 patients were identified.The median age was 13 years.Of the 24 patients diagnosed with pilomatricoma,14(58.3 %) were female.In all cases,the initial presentation was an asymptomatic,slow growing,superficial hard mass with bluish discolouration.The most common sites of occurrence were the upper limbs(45.8 %),face(20.8 %) and preauricular region(12.5 %).The size of the surgical specimens collected ranged from 0.4 to 2.5 cm.The diagnosis was confirmed by histopathological examination.Ghost cells and basaloid cells were described in most of the cases.There were no recurrences in this series.
Conclusion: This entity should be considered with other benign or malignant conditions in the clinical differential diagnosis of solitary firm skin nodules,especially those on the face,neck and upper limbs.The diagnosis can generally be made by clinically.The treatment of choice is surgical excision,and the recurrence rate is very low.

PS-06-029
Immune response in squamous cell carcinoama (SCC): Tumoural microenvironmental study
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Objective: The classical theory said that an intact immune response is important to preventing and inhibiting tumour development. There are only few studies related with the immune system pattern in the skin cancer. Most of all have been done in the skin malignant melanoma. The aim of our study was to identify and analyze the immune response profile in the squamous cell carcinoma microenvironment.
Method: The study is a retrospective-type and are 35 cases included in it from 2016, random choose from the file of Marghita Hospital Pathology Department. Two skill pathologist review the cases diagnosed with squamous cell carcinoma, previously stain with hematoxilin eosin. All the cases are labeled with CD3 and CD20 by immunohistochemistry technique. (Bechmark XT, Ventana Medical Systems Inc.,USA)
Results: The average values of T and B lymphocyte populations from the intratumoural areas are 434 respectively 127, the T/B ratio is 3.42. In the peritumoural areas, the average values for lymphocytes T and B are 778 respectively 337, 2.3 is T/B ration.
Conclusion: According with our data the cellular immune response is more important in the intratumoural areas, but overall the higher number of T cell are seen in peritumoural areas (peritumoural T cell/intratumoural T cell = 1.79)

PS-06-030
Basal cell carcinoma of external auditory canal: A rare complication of long-lasting systemic lupus erythematosus
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Objective: Malignant tumours of external auditory canal (EAC) are very rare, with an estimated annual incidence of 1-6/1.000.000. The most common type is squamous cell carcinoma, followed by adenoid cystic carcinoma, basal cell carcinoma (BCC) and melanoma. Exposure to cytotoxic and immunosuppresive agents as treatment in systemic lupus erythematosus (SLE) combined with immune system defects increases overall malignancy susceptibility.
Method: We present the case of a 56-year-old man with long personal history of SLE (24 years) associated with Sjogren syndrome, and coagulation abnormalities. At presentation he had two reddish ulcerative and asymptomatic plaques, each in every EAC and multiple painful purplish nodules in fingers in evolution of 1 year.
Results: A fungating mass located in the left ear's EAC, measuring 2,2 cm, was found. A biopsy of the tumour mass was performed revealing a BCC, therefore the patient underwent a surgical removal of external ear with the external segment of EAC harboring the tumour. Final histopathological diagnosis was nodular and infiltrative BCC, pT2Nx, completely removed.
Conclusion: Patients with SLE have a higher incidence of developing non-melanoma skin cancer with a significant risk after 20 years of disease. Therefore, SLE patients should be carefully monitorized for skin malignancies in order to avoid mutilating surgery of head and neck.

PS-06-031
Compound melanocytic nevus with lymphatic embolus of nevus cell. A rare finding
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Objective: We present a case of compound melanocytic nevus with a lymphatic vessel embolus composed of nevus cell aggregate.
Method: A 40-year old female with no previous history presented with a pigmented nodule on the lower back. The clinical diagnosis of melanocytic nevus was made. Grossly, the resected specimen consisted of elliptical skin with a slightly raised brown nodule measuring 0.5 cm in maximum diameter and 0.1 cm in height.
Results: On microscopic examination a compound melanocytic nevus was identified. The junctional component consisted almost exclusively of melanocytic nests with very few scattered single cells. The intraepidermal component consisted mainly of nests of Type A and Type B cells without atypia or mitotic activity. A number of the nests both junctional and intraepidermal contained melanin pigment. In the upper dermis an aggregate of nevus cells was found within a lymphatic vessel lined by a single layer of endothelial cells. In the deeper sections performed for immunohistochemistry both nevus cell aggregate and vessel disappeared.
Conclusion: The diagnosis of compound nevus with lymphatic nevus cell aggregate was made. Intralymphatic nevus cell aggregates are an

exceedingly rare finding with a very limited number of cases reported in the English literature.

PS-06-032

Cutaneous involvement in T-lymphoblastic lymphoma: Case report

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Objective: Lymphoblastic lymphoma (LBL) is a rare form of non-Hodgkin's lymphoma (NHL). Cutaneous LBL is seen in less than 20 % of patients. The authors reports a case of cutaneous LBL and point out the importance of immunohistochemistry in the differential diagnosis.
Method: A 30 year old man with a history of LBL treated with CHOP sinc 2 years with a complete response presented to the department of dermatology for reddich macular lesions of the trunk. Clinical impression was toxidermy and a punch biopsy was performed. Histolgical examination showed a dermal peri-vascular, abundant atypical lymphoid infiltrate. Atypical lymphoid cells expressed CD3, CD99 and TDT.
Results: In this case, the histological and immunohistological findings concluded to a cutaneous recurrent T-cell lymphoblastic lymphoma.
Conclusion: There have been 14 reported cases of LBL with cutaneous involvement; most of these patients were young and presented multiple cutaneous lesions associated with numerous peripheral adenopathies, invasion of the bone marrow, and in many cases, a mediastinal mass. The clinical presentation of LBL-T in our case is novel on account, it was clinically atypical and it was the only site of recurrence.

PS-06-033

Trichoblastic carcinoma: Clinical and histopathological features

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Objective: The authors report their experience in the clinical and histological findings of the Trichoblastic carcinoma(TC).
Method: Retrospective study of the histologically proven cases of TC, diagnosed between 2006 and 2017 in the Pathology Department of La Rabta's Hospital. Clinical data were reviewed for each patient.
Results: A total of 8 patients with histologically proven TC were investigated. The gender ratio was 1.6 for a male predominance. The average age was 65.3 years. Clinical manifestations were presented as assymptomatic deep dermal nodules. The tumours were seen in the head and neck region in 6 cases (3 on the orbit; 1 on the nose; 1 on the scalp and 1 on the cheek) in the back in one case and in the shoulder in the last case. Histopathological examination confirmed the diagnosis in all of the cases. One case was marqued by the presence of a sarcomatoid changes and vascular emboli. No recurrence were noted in the follow up.
Conclusion: TC is a rare malignant adnexal tumour. Its presentation is non-specific and tits diagnosis is always histological. Histological diagnosis is difficult due to its similarities with other neoplasms and the immunohistochemical study is not of a help.

PS-06-034

Microcystic adnexal carcinoma: A wolf in sheep's clothing

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Objective: Introduction Sclerosing adnexal tumours present a significant differential-diagnostic problem. Predilection of these tumours for head and neck area and selection of the optimal treatment make accurate diagnosis essential.
Method: Case presentation A 74-year-old Caucasian woman with a 10-year history of multiple recurrencies of the upper lip tumour presented with a fast-growing lesion in the scar area. The primary lesion was misdiagnosed as desmoplastic trichoepithelioma (DTE) and all subsequent lesions were considered recurrent DTEs.
Results: Histopathology Histopathological examination revealed a similar pattern in all specimens. A poorly circumscribed tumour invading deeply into the dermis and subcutis was composed of nests of atypical basaloid cells forming glandular structures embedded in abundant hyalinized stroma with perineural and intramuscular invasion. Immunohistochemical analysis revealed CK 5/6, CK 7, p63, CD10, CKHMW and S100 positivity, scattered cells were CEA and CD5 positive, and BerEP4 and Androgen receptor were negative. Stromal cells revealed mild positivity with CD34. Ki67 < 5 %. Histological and immunohistochemical pattern was consistent with microcystic adnexal carcinoma.
Conclusion: To date no immunohistochemical markers of sclerosing adnexal tumours have been described to provide sufficient sensitivity and specificity for diagnosis, but combination of histologic characteristics and particular immunohistochemical markers may aid in the distinction of MAC from other sclerosing lesions.

PS-06-035

Association of Hedgehog signal expression with MCPyV infection and outcome in Merkel cell carcinoma

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Objective: Merkel cell carcinoma (MCC) is an aggressive neuroendocrine skin cancer and Merkel cell polyomavirus (MCPyV) was detected in approximately 80 % of this cancer, and MCPyV T-antigen play an important role in carcinogenesis of MCC. Hedgehog signaling is a developmental pathway in human embryogenesis and organogenesis, and aberrant overexpression of Hodgehog signal molecules was reported in several cancers. We investigated the association of Hedgehog signaling expressions with MCPyV infection or prognosis in MCCs.
Method: 29 MCPyV-positive and 21 MCPyV-negative MCC samples were immunohistochemically analyzed with antibodies for SHH, IHH, PTCH1, SMO, GLI1, GLI3. Sequencing for SHH exons and GLI1 exons was performed.
Results: Expression of SHH was stronger in MCPyV-positive MCCs than -negative MCCs ($p < 0.001$). Higher GLI1 expression, MCPyV presence, male and the yellow race were significantly associated with better overall survival ($p = 0.034$, $p = 0.001$, $p = 0.042$, $p = 0.036$, respectively). Higher SHH expression and MCPyV infection were statistically associated with better MCC-specific survival ($p = 0.037$, $p = 0.002$, respectively).
Conclusion: Higher expressions of SHH and/or GLI1 may be prognostic markers for better survival in MCCs.

PS-06-036

Primary cutaneous gamma-delta T-cell lymphoma (PCGD-TCL) presenting as lupus erythematosus panniculitis (LEP): A case report

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Objective: PCGD-TCL is a rare entity (<1 % of all skin lymphomas) that generally presents with disseminated plaques and/or ulceronecrotic nodules and aggressive clinical course. Histologically, PCGD-TCL shows

epidermotropic, dermal and/or subcutaneous infiltrates, or combinations of these patterns. Morphologically, LEP can mimic PCGD-TCL and a significant overlap between both entities has been reported.
Method: We present a case of a 63-year-old woman with a first biopsy resembling LEP, which eventually showed aggressive clinical course
Results: The patient consulted with a two-months history of an asymptomatic subcutaneous nodule on her thigh. A first biopsy revealed vacuolar interface changes, mucin deposition within the dermis, and a mostly lobular inflammatory infiltrate of the subcutaneous fat, admixed with basophilic sclerosis. A histologic diagnosis of LEP was suggested. During the next 9 months, the patient developed new lesions, some of them showing spontaneous ulceration. Overall status worsened, and fever and leucopenia were detected. A new biopsy from an ulcerated lesion revealed an atypical lymphoid infiltrate. The neoplastic cells were CD3+,CD56+,granzyme+,perforin + and TCRgamma + with high ki67 (70 %). CD20,CD4,CD8,CD30,TCRBF1,PD1,EBV-LMP1 and EBER were negative.
Conclusion: Given the poor prognosis it conveys, PCGD-TCL needs to be carefully excluded in any worrisome looking panniculitic infiltrate. Distinction between LEP and PCGD-TCL may be particularly challenging.

PS-06-037
Altered expression of SWI/SNF complex and its significance in Merkel cell carcinoma
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Objective: Merkel cell carcinoma(MCC) is a clinically aggressive neuroendocrine skin cancer and 80 % cases are associated with Merkel cell polyomavirus (MCPyV). Pathogenesis of MCCs have still not been well elucidated. SWI/SNF (SWItch/Sucrose Non-Fermentable) complexes regulate gene expressions by ATP-dependent chromatin remodeling processes that are critical for differentiation and proliferation and SWI/SNF gene expressions frequently altered in human cancers. We investigated the association of altered expression of SWI/SNF complex with prognostic and biological significance in MCCs.
Method: We analyzed the immunohistochemical expressions of INI1, BRG1, BRM and ARID1A in 30 MCPyV-positive and 20 MCPyV-negative MCCs.
Results: All MCC cases showed INI1 and ARID1A expression, whereas 5 cases had loss or reduced BRG1 expression and 2 cases had reduced BRM expression. There were no statistically significant differences between altered expressions of SWI/SNF complex such as BRG1 and clinicopathological factors including MCPyV-infection and prognosis. Interestingly, Contiguous squamous cell carcinoma (SCC) foci in 3 combined MCCs showed no or reduced BRG1 expression.
Conclusion: Our study indicated that loss of SWI/SNF function is occasionally related to MCC and is not associated with MCPyV-infection and prognosis. However, different BRG1 expressions between MCCs and SCCs may be reflected by different oncogenic mechanism in these lesions.

PS-06-038
The expression of Glut-1 in malignant melanoma and melanocytic nevi: An immunohistochemical study of 400 cases
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Objective: Glucose transporter-1 (Glut-1) is a cell membrane glycoprotein involved in glucose uptake and overexpression of Glut-1 is important cell adaptation mechanism against hypoxia. Upregulation of Glut-1 can be found in several malignant tumours, which are able to reprogram their metabolism from oxidative phosphorylation to aerobic glycolysis (Warburg effect). However, the data regarding melanocytic lesions is equivocal.
Method: Comprehensive immunohistochemical analysis of Glut-1 expression was performed in 225 malignant melanomas (MM) and 175 benign nevi. H-scoring system was used for more precise quantification of membranous Glut-1 expression.
Results: The expression of Glut-1 (cut-off for positivity was H-score 15) was found in 69/225 MMs. Number of positive cases increased with higher Breslow thickness ($p < 0.0000$) comparing groups <1 mm (10/100;10 %), 1–3.99 mm (33/91;36 %), and ≥4 mm (26/34;76 %). All benign nevi were classified as negative (Glut-1 expression of median H-score 2 was detected in 24/175;13.7 %).
Conclusion: Membranous Glut-1 expression is common feature of MM but it is very rare in benign melanocytic nevi. Our results suggest membranous expression of Glut-1 as a surrogate marker for assessing biological nature of benign and malignant melanocytic lesions. However, despite high specificity, sensitivity of this marker is relatively low.
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PS-06-039
Thirteen years of follow-up and multiple neoplasms in two siblings with Muir-Torre Syndrome
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Objective: Muir-Torre Syndrome (MTS) is a rare autosomal dominant genodermatosis (approx. 200 documented cases), characterized by the coexistence of sebaceous neoplasms with one or more visceral tumours. It is associated with loss of expression of DNA reparatory proteins (hMLH1, hMSH2 and hMSH6 genes), and is therefore considered by some a subtype of the Lynch syndrome.
Method: We present the cases of two siblings, both of which have developed sebaceous neoplasms in combination with various internal organ tumours, over a period of more than 13 years.
Results: Immunohistochemical studies revealed loss of expression of MSH2 and MSH6 proteins in all but one of the lesions in both patients. Thus, they are diagnosed with MTS and are being closely followed-up.
Conclusion: We consider MTS to be an entity of particular interest, because of the central role of pathologists in screening, early detection and prevention of morbimortality due to this clinically important syndrome.

PS-06-040
Expression of CD 30 and PD-1 in mycosis fungoides: Diagnostic and prognostic implications
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Objective: Mycosis fungoides (MF) is the most common type of cutaneous T cell lymphoma. MF is characterized by the presence of CD3+ T lymphocytes that most of the cases express a T helper phenotype (CD4+). An increased CD4/CD8 ratio is often observed. PD-1 is one of the T-follicular helper lymphocyte markers which has been expressed in several cutaneous T- cell lymphomas including MF. In this study we investigated CD3, CD4, CD8 expressions in addition to PD1 and CD30 expression for the diagnosis and prognosis in early MF.
Method: We have reviewed 119 skin biopsies diagnosed as MF at Gazi University Department of Pathology between 2008 and 2015. CD3, CD4,

CD8, PD-1 and CD30 expressions were evaluated in formaline fixed paraffin embedded tissues by immunohistochemistry. CD3, CD4 and CD8 expressions were evaluated in intraepidermal and dermal lymphocytes separately and staining percentages were recorded. Membranous staining of CD30 and PD-1 more than 10 % was considered positive and recorded as staining percentage.
Results: Diffuse CD3 expression in intraepidermal and dermal lymphocytes was observed in all of the cases. Intraepidermal and dermal CD4/CD8 ratio was increased in 113 of 119 cases. CD30 expression was observed in 22.6 % of the cases. CD30 expression was not related with recurrence. PD-1 was positive in 22 % of cases and PD-1 positivity was significantly related overall survival.
Conclusion: Although we couldnt demonstrate the prognostic impact of CD30 in our study; PD-1 expression could be the marker for agressive clinical behavior. Also PD-1 expression may bring new treatment option in MF.

PS-06-041
Squamous cell carcinoma (SCC) arising on giant condyloma acuminatum: Five cases with HPV status
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Objective: To investigate the incidence of high-risk HPV infection in giant condyloma acuminatum(GCA)
Method: Lesions diagnosed as GCA between 2007 and 2016, were re-evaluated. Cases with in situ and/or invasive squamous cell carcinoma nearby the typical condylomatous areas were selected. p16 (clone G175-405; 1/10) immunohistochemistry was applied on sections harboring both areas. Fourteen high-risk HPV types (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) were tested by using the Genotype Real-TM Quant Kit according to manufacturers' instructions.
Results: Five male patients with a mean age of 55 were included in the study. Two of them had penile and 3 had perianal lesions with a mean size of 16.8 cm. Mean time lapse between the emergence of the lesion and date of surgery was 8.8 years. Adjuvant radiotherapy was the treatment of choice in 1 case, along with surgical excision. Mean follow-up period was 37 months; all patients were alive without recurrence and /or metastasis. Areas of invasive (2 cases)/in situ (3 cases) carcinoma were highlighted by p16 staining. HPV type-16 was detected in all cases.
Conclusion: Carcinoma may develop on GCAs presenting with a long history. We think that high-risk HPV may have a role in this transformation.

PS-06-042
Glandular peripheral nerve sheath tumour: An unusual case
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Objective: The presence of true glandular structures in peripheral nerve sheath tumours (PNST) is rare. Most of the reported tumours are malignant PNSTs, but some are schwannomas. We herein present a case of glandular PNST with neurofibroma-like features.
Method: A 37-year-old pregnant woman who had no evidence of neurofibromatosis presented with a lump in front of the left ear 1 cm in diameter. The lesion had existed since childhood and did not show any significant growth or change. Total excision was performed.
Results: Histopathological examination revealed a tumour containing a spindle cell component resembling neurofibroma and haphazardly distributed glandular component extending to deep dermis among the spindle cells. The glandular component was lined by a single or two layers of non-ciliated cuboidal or columnar cells appearing like syringoid neoplasia. Mitotic figures and cytological atypia were not observed. Immunohistochemically, spindle cells were positive for S-100 and CD34, while glandular cells were stained with pan-cytokeratin, p63 and focally EMA.
Conclusion: Owing to the fact that a few of similar cases have been reported, the biologic behavior for such a lesion is unknown. However, we suggest that the lesion might be benign because of the long-standing clinical history and no obvious histologic evidence of malignancy.

PS-06-043
Clinical-pathological and immunohistochemical features of Merkel cell carcinoma
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Objective: We correlate clinical-pathological and immunohistochemical features of Merkel cell carcinoma (MCC) with Merkel cell Polyomavirus (MCPyV) infection. MCC is a rare and aggressive neuroendocrine neoplasm of the skin; the majority of them are associated with the MCPyV infection.
Method: A total of 29 MCC diagnosed between 1991 and 2016 in the Pathology Department of Sassari's University were investigated. We analyzed new sections from formalin fixed paraffin embedded specimens of all primitive skin lesions of our archival material. The viral infection was detected by immunohistochemistry.
Results: Fifty-nine percent were positive for MCPyV LT antigen. All cases of MCC of the upper extremities (3/3) and 75 % (3/4) of the trunk were associated with viral infection. We investigated the tumour associated lymphocytic infiltrate; interestingly the only two cases with massive lymphocytic infiltration were positive for MCPyV and both patients were alive after 107 and 56 months of follow up. Ten cases showed necrotic areas and eight of these were virus positive.
Conclusion: MCPyV infection seems to be correlate to specific sites (upper extremities and trunk), massive lymphocytic infiltration and necrosis. These findings seems to suggest a possible strong protective immune reaction probably viral induced. We didn't find any correlation between sun-exposed areas and virus infection.

PS-06-044
Glomeruloid hemangiomas as the first symptoms of Castleman's disease
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Objective: Glomeruloid hemangiomas are usually associated with Castleman's disease and POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M-protein and skin changes). They are considered a reactive vascular proliferation and play an important role as a specific marker in a proper diagnosis. We report a case of Castleman's disease with POEMS syndrome, since it is a rare lesion and its first morphological symptoms must be evaluated carefully.
Method: A 38-year-old man was presented 2 years ago with numerous vascular papules on the trunk and pain in the fingers of the left foot. Biopsies were performed and capillary hemangiomas were identified. In one and half year this patient was admitted to the hospital with weight loss, low-grade fever, lymphadenopathy, ascites, hepatosplenomegaly, superficial distal hypoesthesia in the feet and hands, walking difficulties, gynecomastia. Histological and immunohistochemical studies of cervical lymph nodes were performed and preliminary biopsies of hemangiomas were reexamined.
Results: A histological review of the hemangiomas identified dilated vascular spaces in the dermis, containing in their lumens coiled capillaries

resembling a renal glomerulus. These capillaries were lined by a single layer of endothelial cells with swollen clear nuclei, suspicious on the viral damage. The single small vessels close to such spaces had the same endothelium. These cells were negative for HHV8 and expressed VEGF. In lymph nodes there was an angiofollicular hyperplasia with some clusters of plasma cells in the interfollicular parenchyma. Multicentric Castleman's disease with POEMS syndrome was diagnosed.
Conclusion: This case suggests the opinion that glomeruloid hemangiomas can be a first specific marker of multicentric Castleman's disease with POEMS syndrome. Accounting for these signs may allow starting a specific treatment earlier.

PS-06-045
Experience of application immunofluorescence antigen mapping for morphologic diagnosis of different types of congenital epidermolysis bullosa
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Objective: to optimize the morphological diagnosis of different types of CEB.
Method: 28 skin biopsies from 14 patients with different types of CEB were investigated. The investigators performed histological examination of skin fragments taken from a bullous area and immunofluorescence antigen mapping using the indirect immunofluorescence test (IIFT) with antibodies against structural proteins of the dermal- epidermal junction (laminin $\alpha 3$, $\beta 3$, and $\gamma 2$ chains, keratins 5 and 14, types VII and XVII collagen, $\alpha 6$ and $\beta 4$ integrin subunits, desmoplakin, plectin, kindlin-1, and plakophillin) of the apparently unaffected skin.
Results: Immunofluorescence antigen mapping could determine the type of CEB in all cases and in 86 % of cases identify the protein, the impaired production of which was responsible for the development of the disease.
Conclusion: Immunofluorescence antigen mapping is an integral part of the comprehensive morphological diagnosis of CEB, acting as an intermediate between the morphological verification of CEB diagnosis and the targeted search for mutations by a molecular genetic method.

PS-06-046
Investigation on the effects of melanin exposure on macrophages: A preliminary study
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Objective: The tumour microenviroment is a complex biological system made up of different types of cells, each one with a different impact on prognosis. Tumour-associated macrophages are characterized by the ability to switch from a M1-like "anti-tumour" activation status to a M2-like "pro-tumour" immunosuppressive status. In melanoma, melanin-containing macrophages ("melanophages") are often present in the tumourmicroenvironment, but their role in the local immune response is unknown, and studies on the effects of melanin loading of macrophages are lacking.
Method: We tested the effects of synthetic melanin on a mouse monocytic cell line (J774.2) and on peripheral blood-derived CD14+ monocytes from two different patients. We used flow cytometry, ELISA and bioenzymatic assays to compare the effects of melanin with LPS stimulation on cell viability, phagocytic activity, HLA-DR and CD206 (a classical M2-macrophage marker) expression, and TNFalfa and IL-10 production.
Results: Macrophage viability was not affected by melanin exposure, while both LPS and melanin decreased phagocytosis in macrophages. A trend towards diminished HLA-DR expression and decreased TNFalfa production after exposure to melanin in comparison to LPS exposure was observed.
Conclusion: Preliminary results indicate that melanin exposure induces a decrease of several functions in macrophages.

PS-06-047
BRAF-mutated giant congenital melanocytic nevus with extensive neurotisation and multiple large nodal nevi
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Objective: Large nodal melanocytic nevi mimicking metastatic melanoma and extensive neurotization resembling neurofibromas in giant congenital melanocytic nevus have been very rarely reported. Congenital melanocytic nevi have NRAS or BRAF mutations. Compared to NRAS, BRAF mutations are uncommon in large/giant congenital melanocytic nevi.
Method: We report a 52-year-old woman with a giant congenital melanocytic nevus with multiple lymphadenopathy.
Results: Histological examination revealed extensive neurotization that showed strong positive immunohistochemical staining for S100 protein but showed negative staining for Melan-A. There were capsular and parenchymal nevus cell deposits in lymph nodes. In mutation analysis, BRAF V600E mutation was found, but NRAS Q61 mutation was not detected.
Conclusion: We discuss its clinicopathological, immunohistochemical, and molecular features and the differential diagnosis.

PS-06-048
Cutaneous Rosai-Dorfman disease: Report of 2 cases
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Objective: Although cutaneous involvement in Rosai-Dorfman disease (RDD) is common, purely cutaneous disease is rare and not well documented. The aim of the study was to present two cases of primary cutaneous RDD disease.
Method: Patients were 1 male and 1 female, 40 and 59 years old, respectively. The first of the lesions was presented as papule located in the breast skin with the clinical diagnosis of eczema or paget disease. The second one as nodule located in the head with the clinical diagnosis of dermatofibrosarcoma protuberans or fibrous histiocytoma. Physical examination and CT showed no lymphadenopathy or any extra-cutaneous lesions.
Results: Histology revealed polygonal S100+ histiocytes showing emperipolesis (lymphocytes, erythrocytes) and many lymphocytes, plasma cells and neutrophils. The immunohistochemistry showed that the histiocytes were also positive for CD68 and negative for CD1a, FXII, langerin and plasma cells were polyclonal. The patients remained asymptomatic with no signs of recurrence or other extranodal sites or associated lymphadenopathy 9 months after surgery.
Conclusion: RDD with extranodal involvement occurred in 43 % of the cases, with skin being the commonest site. A panel of immunohistochemical markers is essential to make the differential diagnosis from other histiocytoses.

PS-06-049
A curious case of chest rash: Cutaneous plasmocytosis, a case report
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Objective: Cutaneous plasmacytosis is a rare lymphoplasmacytic disorder of unknown cause, reported mainly in middle-aged Japanese men; 11 cases have been reported in the white population.
Method: Sixty-seven year old male with chief complaint of chest rash for 4 years. 2012: Patient presented for first time with chest rash. A punch biopsy was performed. 2014: Patient presented again for violacious small patches and nodules on the chest.
Results: Punch Biopsy 2012: Moderately dense, perivascular infiltrate of plasma cells without atypia in the superficial and deep dermis and small numbers of lymphocytes and histiocytes. Dermal fibrosis. Skin rib cage, biopsy (2014). Changes suggestive of Cutaneous Plamocytosis
Conclusion: Cutaneous plasmocytosis is a rare benign entity. The age rate is 20 and 62 year old. Cutaneous plasmocytosis is characterized by red/brown poor circumscribed plaques, macules and nodules occurring mainly on the trunk. This entity can be accompanied by hypergammaglobulinemia, lymphadenopathy, fever and anemia. Cutaneous plasmocytosis is histopathologically characterized by dermal perivascular infiltrates of mature polyclonal plasma cells with some lymphocytes and histiocytes. Special Stains/ Immunohistochemistry: Kappa and Lambda inmunostains shows a mixed polyclonal population of plasma cells. There is not definite treatment guideline for cutaneous plasmocytosis.

PS-06-050
A case of pleomorphic dermal sarcoma metastatic to regional lymph node and parotid gland
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Objective: Pleomorphic dermal sarcoma is a rare malignant tumour which has similar pathological findings with atypical fibroxanthoma, and additional features such as invasion of deep subcutaneous tissues, tumour necrosis, lymphovascular or perineural invasion.
Method: An 81-year old woman presented with an ulceronodular circumscribed lesion of 20 mm in maximum diameter, located left cheek. Surgical excision was performed.
Results: Histopathological examination revealed large, ill-defined, dermal based and asymmetrical tumour with infiltrative growth and extension into deep subcutaneous adipose tissue and skeletal muscle. Tumour cells were epithelioid shaped with an abundant eosinophilic cytoplasm and pleomorphic, centrally located vesicular nuclei containing prominent one or multiple nucleoli. They were intermingled with sparse spindle-shaped tumour cells. Mitoses were numerous. Ulceration was present, but tumour necrosis, lymphovascular invasion and perineural infiltration were not seen. Proliferating actinic keratosis was observed in the overlying epidermis. Immunohistochemically, tumour cells expressed CD10, Vimentin. Staining for pan-cytokeratin, p63, cytokeratin5/6, EMA, CEA, S-100, Melan-A, Actin, Desmin and CD31 were negative which ruled out carcinoma, melanoma, leiomyosarcoma and angiosarcoma. Subsequently, a functional neck dissection and partial parotidectomy were performed. Metastasis to parotid gland and a cervical lymph node were detected.
Conclusion: We present this case because it is rare entity that deserves accurate diagnosis.

PS-06-052
Protothecosis skin lesion - a case report
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Objective: Protothecosis are uncommon infections caused by Prototheca, an achlorophylous algae. Clinically it can be manifested as cutaneous lesions, olecranon bursitis or systemic protothecosis. We report a case of cutaneous protothecosis, not suspected clinically.
Method: Patient was a 74 year old female immunocompromised (corticotherapy plus cyclosporine), with a clinically history of Sezary syndrome. She presented with pulmonary lesions suggestive of an infectious process and cutaneous ulcerative papules on upper extremities. A skin biopsy was performed to rule out mycoses fungoides, molluscum contagiosum or xanthoma.
Results: Histology revealed an ulcerative dermic lesion composed of a granulomatous mixed inflammation and the presence of numerous structures characteristic of mature sporangia of Prototheca, positive for PAS, Grocott and Giemsa.
Conclusion: Prototheca spp. exist in the environment on detritus and contaminants of various substrates. How they cause human disease is unknown. They are considered as opportunistic agents. With an increase of immunocompromised individuals in our days, infections by this unusual organisms is prone to increase. Because the disease is not clinically suspected, patients usually undergo unnecessary treatment. The identification of the organism is important, as medical treatment is controversial and most skin lesions are better treated with surgical excision.

PS-06-054
Epidermotropic skin metastasis from urothelial carcinoma of the bladder: A case report
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Objective: Cutaneous metastases from bladder malignancies are rare.
Method: We report a case of a 74 year old man who underwent cystoprostatectomy and adjuvant chemotherapy for a pT4a N- bladder urothelial carcinoma. Five years later, he presented with verrucous and erythematous plaque lesion near ureterostomy site on the lomber skin.
Results: Skin punch biopsy confirmed epidermotropic cutaneous metastasis from urothelial carcinoma.There weren't isolated tumour cells in the dermis. Excision of the lesion was performed. Histopathological examination showed that papillary and pagetoid urothelial carcinoma infiltration in the epidermis. İmmunohistochemically epidermotropic tumour was strongly positive with CK7. Focal staining were observed with EMA and CK20. CEA was negative. Patient died 1 years after diagnosis of the metastatic tumour.
Conclusion: Metastatic infiltration of the skin may occur due to direct tumour invasion, hematogenous or lymphatic spread, or as a result of iatrogenic implantation of tumour cells. Metastatic involvement of the epidermis is exceedingly rare. Tumours that are known to occasionally metastasize and colonize in the epidermis include cutaneous adnexal carcinoma, mammary and extramammary Paget's disease and malignant melanoma. There were isolated case reports about epidermotropic skin metastasis from breast, lung, vulva, cervix, stomach, colon, salivary gland carcinomas and sarcoma. A histologic feature unique to this case was epidermotropism, previously not noted in metastatic urothelial carcinoma.

PS-06-056
Coexistence of pilomatricoma and epidermal cyst (follicular hybrid cyst) in two patients: Case report
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Objective: Pilomatricoma is a benign tumour derived from the hair matrix and cortex. Epidermal cyst of the skin is very common lesion, considered to be derived from the follicular infundibulum. In literature review, we found that coexistence of pilomatricoma and epidermal cyst's extremely rare. We present two cases in which pilomatricoma was associated with epidermal cyst.

Method: Case 1 is 16-year-old female with a painless mass in the left arm of the skin. Case 2 is 28-year-old female with a painless mass in the right arm of the skin. Both of the lesions had been present for 1 year and had been increased in size gradually.
Results: In gross examination, both of the lesions were grayish-brown colored and showed a cystic appearance. Histologically, the lesions had two different components; one showed the feature of epidermal cyst and another composed of significant ghost cells, focal basaloid cells and calcification. Surrounding the lesions, chronic inflammatory reaction was noticed.
Conclusion: Follicular hybrid cyst (FHC) which includes any types of cyst arising from the various parts of the pilosebaceous unit. Pilomatricoma coexistent with epidermal cyst may be associated with Gardner's syndrome. We present two cases that none of the patient had any signs of Gardner's Syndrome.

PS-06-057
Cutaneous sarcoidosis: Clinicopathologic study of 22 cases
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Objective: Sarcoidosis is a multisystem granulomatous disorder of unknown aetiology. Cutaneous involvement is found in more than 30% of cases. This study aimed to describe the charateristic clinicopathologic features of cutaneous sarcoidosis.
Method: We conducted a restrospective study of biopsy-proved cases of cutaneous sarcoidosis diagnosed over a period of 6 years at our department. The diagnosis of systemic sarcoidosis was made according to conventional criteria.
Results: Our study included of 22patients, aged 17–80 years (mean 51,22 years), of whom 86,4 % were females. Systemic involvement(unique or multiple) was detected in 86,4 %: lung (72,7 %), lymph nodes(72,7 %), sinus(13,63 %) and liver(0,9 %). Cutaneous lesions revealed the disease in 68,18 % of cases. Most skin lesions were the papulonodular type (68,18 %) and located in the face (72,72 %). Laboratory investigations revealed high calcium levels (50 %), high angiotensin-converting enzyme concentrations (50 %). The histology was characterized by infiltration granulomas in the dermis and/or the subcutis associated to fibrinoid necrosis (0,9 %). In 17 patients, the cutaneous lesions remitted spontaneously under cortisone therapy in less than 2 years
Conclusion: The skin lesions of sarcoidosis are classified as specific and non-specific. Although two biopsies with granulomas are theoretically necessary to make the diagnosis of sarcoidosis, a skin biopsy showing typical feature of non-caseating granulomas often obviates the need for additional organ biopsies.

PS-06-058
Merkel-cell carcinoma diagnosed in Central Universitary Hospital of Asturias: Review of clinicopathological characteristics with prognosis interest
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Objective: Merkel Cell Carcinoma (MCC) is an agressive cutaneous neuroendocrine carcinoma. There are few studies of large series or prospective studies because it is a very infrequent tumour.
Method: A review of 31 cases diagnosed in our institution between 1977 and 2016 was performed. Clinicopathological and immunohistochemical features that had been previously described to have prognostical implications were revised.
Results: Clinical features: 60 % of the cases were women, with a medium age of 75 years and mainly head and neck located. Most of them were diagnosed in stages IB (30 %) and IIB (40 %). During follow up 42 % developed metastases, 19 % recurrences and 47 % died. Pathological features: Medium size was 3 cm, 48 % have nodular architecture, 70 % reach subcutis, medium thickness was 13 mm, 47 % had lympho-vascular invasion, and an average of 14 mitosis/5 HPF. Sixty-one percent showed associated inflammatory infiltrate. 100 % were CK20 positive, 94 % CD56 and 70 % p63. There was a higher metastatic risk in tumours expressing p63 [OR = 9,6(1,2–90,3)] and lower in patients with associated inflammatory infiltrate [OR = 0,18(0,04–0,86)]. Overall survival depended on diagnostic stage.
Conclusion: A high percentage of the sample are Merkel cell Polioma Virus related (91 %). We noticed that the only clinicopathological features related with poor prognosis were diagnostic stage, p63 expression and lack of inflammatory infiltrate.

PS-06-059
Trichoblastic carcinoma of the face; A case report
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Objective: Trichoblastic carcinoma(TC) is a rare malignant adnexal tumour originating from the hair germ-cells. It can thrive from trichoblastoma; therefore is also named as Malignant Trichoblastoma. It usually presents on the scalp, face, lip, alar-region, vulva, eyelid, and coccyx.
Method: Our patient was a 51-year-old man admitted to surgery clinic with a fast-growing, painfull, ulcerated-bleeding mass with a diameter of 1,5 cm on left-preauricular region. He had no personal or family history of underlying skin diseases or malignancies. The punch biopsy done from the lesion showed it was a malignant skin-adnexal tumour. So the lesion was completely excised with 0.5 mm of surrounding normal skin.
Results: The histopathological evaluation revealed multiple basaloid epithelial(Pancytokeratin-positive) tumour nodules located in the dermis with no-connection to the epidermis. The nuclei of the tumour cells arranged in a palisaded-fashion, were pleomorphic, hyperchromatic with some prominent nucleoli and many mitosis. Infiltrative areas with smaller islands of tumour cells were found in adjacent-tissues. The stroma condensing around tumour lobules comprised stellate/spindled fibroblasts staining positive with CD10. As ki-67 index was; the mass was diagnosed as high-grade TC.
Conclusion: TC is a rare malignant neoplasm and surgical excision is the treatment. Although only a-few metastatic cases have been reported, close follow-up is essential.

PS-06-060
Spindle cell melanoma like malignant peripheral nerve sheath tumour
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Objective: Spindle cell melanoma (SCM) is an uncommon form of melanoma that may be confused histologically with other tumours, including malignant peripheral nerve sheath tumours (MPNST).
Method: Case report: A 63-years old man presented with a subungual lesion of the first finger of the left foot, which is solved as granulation tissue, in another institution. The second opinion of this lesion included spindle cell tumour possible origin Schwann cells, but I did not rule out the possibility of spindle cell pigmented lesion.
Results: Discussion: A subsequent excisional specimen demonstrated a relatively ill-circumscribed nodule. The epidermal and superficial components consist of rounded epithelioid cells with amphophilic cytoplasm and vesicular nuclei while the remainder of the tumour, more deeply, consists of fascicles of more palely eosinophilic spindle cells with a

prominent neural-like fascicular pattern and also having vesicular nuclei. There is strong and diffuse immunopositivity for S-100 protein and SOX10 in both components, far greater than one would see in MPNST, while only the epithelioid component is immunopositive for MART-1 and PNL2.
Conclusion: The inguinal lymph node biopsy shows lymph node extensively replaced by a spindle cell malignant neoplasm with similar morphology to that on the foot and again showing strong and diffuse positivity for S-100 protein and SOX10, negative for MART1 and HMB45 leaving no doubt that this represents metastatic spindle cell malignant melanoma.

PS-06-061
Expression of c-KIT in malignant melanoma subtypes: An immunohistochemical study
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Objective: Distinct genetic aberrations of KIT in melanomas have been confirmed however the role of immunohistochemistry in the assessment of KIT status is not well established. We aimed to analyse the protein expression of KIT in melanoma subtypes, and to correlate the expression status with clinicopathologic parameters.
Method: Eighty melanomas including four main subtypes were studied with c-KIT immunohistochemically.
Results: Excluding focally stained cases (<10 % of tumour cells), KIT expression was accepted in 40 (50 %) tumours. Twelve of acral lentiginous (48 %), 10 lentigo maligna melanoma (43.8 %), 15 superficial spreading (68.4 %), and eight nodular melanoma (40 %) was positive. In KIT positive tumours the staining was membranous (40 % of positive cases) or membranous and cytoplasmic. KIT expression was present more than 50 % of tumour cells in 77.8 % of positive cases. KIT staining was markedly positive at the peripheral in situ or superficial invasive areas comparing to the deep invasive areas. KIT mutations at 4q12 were searched with RT-PCR and detected in three of them. Two of these were K642E mutation, the other was L576P. Cases with K642E mutation were also immunohistochemically positive. The expression did not correlate with clinicopathological parameters such as location, tumour type, thickness, stage, and mitosis ($p > 0.05$).
Conclusion: In the literature KIT expression was more than KIT mutations in melanomas and this has usually be related with KIT gene amplifications. In order to identify the association between the protein expression and clinicopathological parameters, more studies are needed.

PS-06-062
Comparative study on some oxidative stress parameters in blood of vitiligo patients before and after therapy by two analytical techniques
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Objective: Oxidative stress is a triggering event in the melanocytic destruction and is probably involved in the etiopathogenesis of vitiligo disease. The aim of the present study was to investigate and to compare some oxidative stress biomarkers in blood samples of vitiligo patients before and after therapy by two different methods: Electron Paramagnetic Resonance (EPR) and spectrophotometry.
Method: The study was performed in plasma blood samples in patients with vitiligo: before and after therapy, and compared with the healthy controls. The therapy was: UVB Narrow Band 311 nm phototherapy- 3 times weekly for 6 months period with average cumulative dose 19.5 J/cm3, with antioxidant nutritional supplement for 6 months daily. The products of lipid peroxidation were measured as malondialdehid (MDA), spectrophotometrically by thiobarbituric acid method. The levels of Ascorbate radicals (Asc.) and ROS products were determinated by EPR spectroscopy.
Results: The applied combined therapy to vitiligo patients provokes an increase in the levels of Asc• radicals and ROS products and a decrease in levels of MDA products. Also in all treated patients were observed significant repigmentation.
Conclusion: The antioxidant therapy, enriched with vitamins leads to improvement of the oxidant - antioxidant balance in vitiligo patients.

PS-06-063
Clear cell squamous cell carcinoma (SCC) of skin: A case report
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Objective: Clear cell squamous cell carcinoma (CCSCC) is an extremely rare variant of SCC of skin in which ultraviolet radiation has been suggested as a possible etiology in carcinogenesis. The goal of this case is awareness of squamous cell carcinoma subtypes and differential diagnosis of the other neoplasms.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 84-year- old man with suffering from multiple lesions on his face and neck. At the right preauricular region, the lesion consists of atypical cells which has clear cytoplasm. Histopathological and immunhistochemical results were compatible clear cell squamous cell carcinoma.
Conclusion: Sebaceous neoplasms, clear cell acanthoma, clear cell hidradenoma, clear cell hidradenocarcinoma, tricholemmoma, pilar tumour, balloon cell nevus, balloon cell melanoma, and metastatic renal cell carcinoma should be kept in mind in differential diagnosis due to treatment and prognosis of these neoplasms.

PS-06-064
Cellular neurothekeoma with atypical features
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Objective: Cellular neurothekeomas are benign cutaneous tumours of uncertain histogenesis. Atypical cellular neurothekeoma is a rare neoplasm regarded as a benign tumour. Recurrence is common. We report a single case of cellular neurothekeoma with atypical features.
Method: A 73-year-old woman with a slowly growing mass of her right shoulder. Excisional biopsy was planned. H&E-stained and immunohistochemical studies were performed.
Results: The tumour size was 9 cm. The pathology report revealed a poorly circumscribed dermal tumour with a plexiform growth pattern and extension to subcutaneous fat and skeletal muscle. The tumour composed of nests and fascicles of spindle and epithelioid cells in a background of dense collagen with osteoclastic-like giant cells. Positive immunostaining for MiTF1, CD10 and PGP 9.5. Ki-67 was low. Tumour cells showed mild atypia, mitoses and necrosis.
Conclusion: Cellular neurothekeomas are benign tumours. It's more common in the first three decades of life, with female predominance. The most common anatomic sites are the head and neck, shoulder, and upper extremities. Most tumours are smaller than 2 cm. The main differential diagnosis is a melanocytic tumour. It seems that atypical histologic features in cellular neurothekeomas (large tumour size, necrosis, high mitotic rate, deep involvement and infiltrative growth pattern) are of no clinical significance.

PS-06-065

Kaposi sarcoma: Morphological and immunohistochemical diagnostic methods

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Objective: The differential diagnosis of Kaposi sarcoma (KS) includes many tumours such as dermatofibroma, histiocytoid hemangioma, kaposiform hemangioendothelioma, angiosarcoma.
Method: Biopsy material from seven HIV negative patients (age 45–75 years), 3 women (51, 32 %) and 4 men (48, 68 %), was studied. In 6 cases (72,37 %) patients complained of skin tumours. In 1 case (27,63 %) diagnosis was established post mortem.
Results: Immunohistochemical studies have shown monomorphic expression of CD34 by endothelial cells while expression of Von Willebrand factor was heterogeneous, cells were generally negative for CD31. Endothelial cells and myofibroblast-like cells have shown focal intensive nucleocytoplasmatic expression of HHV8. Myofibroblast-like cells demonstrated intensive Ki-67 positivity. Additional markers IgL(lambda), IgL(kappa), CD38, CD3, CD79a, CD30) were used. Cells demonstrate intensive IgL(lambda), IgL(kappa), CD38 cytoplasmatic expression, CD3, CD30 membrane and cytoplasmatic expression and membrane expression of CD79a.
Conclusion: Pathomorphological diagnostics of KS should include histological study with consideration of chaotic character of angiogenesis, proliferation of spindle cells with endothelial markers, mononuclear cell infiltration, and immunohistochemical study with CD34, CD36, CD31, Von Willebrand factor, and Ki-67. Additional markers (IgL(lambda), IgL(kappa), CD38, CD3, CD79a, CD30) in pathomorphological practice for differential diagnosis.

PS-06-066

Merkel cell carcinoma: A histological and immunohistochemical review of 15 cases

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Objective: Merkel cell carcinoma (MCC) is a rare malignant skin neoplasm with the potential for local recurrence, spreading to regional lymph nodes and distant metastases. MCC rarely appears to arise initially in lymph node propably due to regression of primary skin tumour. We present a series of 15 cases and correlate the immunomorphological features with the prognosis and the presence of polyoma virus.
Method: Patients were 5 male and 10 female, aged between 49 and 90 years. Eight of the skin lesions were located in lower extremities, 1 in the shoulder and 1 in the forearm. Three of them were presented to inguinal lymph node and two of them in cervical lymph node. PET/CT scan was performed and excluded a possible primary site or evidence of metastatic disease.
Results: Histology revealed round to oval nuclei, scant cytoplasm with frequent mitoses. The immunohistochemisty revealed positive staining for CK20, CD56, synaptophysin, NF, focal positivity to chromogranin and was negative for TTF-1 and CK7. In nine cases positive nuclear staining to MCPyV was indentified. No better prognosis in patients with MCPyV positive MCC was found.
Conclusion: The characteristic histological appearances and a panel of immunohistochemical markers is essential to make the differential diagnosis from other small blue cell neoplasms.

Monday, 4 September 2017, 09:30–10:30, Hall 3
PS-07 Digestive Diseases Pathology - Liver and Pancreas

PS-07-001

Pancreatic neuroendocrine tumours: Accurate grading with Ki-67 index on Endoscopic Ultrasound-Guided Fine Needle Core Biopsy (EUS-FNB) specimens using the WHO 2010/ENETS criteria

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Objective: The aim of the study was to determine the diagnostic feasibility and accuracy of Endoscopic Ultrasound-Guided Fine Needle Core Biopsy (EUS-FNB) in the diagnosis and grading of p-NETs (based on WHO/ENETS criteria), comparing preoperative pathological biopsies with final surgical specimens.
Method: We retrospectively reviewed patients with p-NETs who underwent EUS-FNB and subsequent pancreatic resection between 2008 and 2017. Ki67 proliferative index was obtained using automated digital image analysis.
Results: The study included 35 patients, 54.3 % women and 45.7 % men, mean age 56.6 years. The mean pancreatic mass size was 29 mm and the most common location was within the body and/or tail of the pancreas (62.9 %). Tumour grading by Ki-67 assessment could be performed in all cases (100 %). The concordance rate of WHO classification between EUS-FNB and surgical specimens was 85.7 % (30/35), the strength of agreement was considered to be "good" ($k = 0.727$).
Conclusion: EUS-FNB is a highly accurate technique for the diagnosis and grading of p-NETs. There was a good correlation between the Ki67 of EUS-FNB and surgical specimens. Preoperative determination of the Ki-67 proliferation index on EUS-FNB of p-NETs should be systematically reported for an optimal patient management.

PS-07-002

Prognostic significance of histopathological features in solid pseudopapillary neoplasm

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Objective: Solid pseudopapillary neoplasm (SPN) is 0.3–2.7 % of all pancreatic tumours. The aim of this study was to investigate histopathological and clinical features and associations between clinical outcome of this rare entity.
Method: Tumour slides of surgical specimens of 24 cases with SPN diagnosed in our department from January 2000 to December 2016 were retrospectively analyzed.
Results: The mean age was 34.5 years (min. 14, max.66). Of 24 cases, 21(87,5 %) were females. Tumours were located prevalently in pancreatic tail (11 of 24). Median tumour size was 6 cm (range, 2–15 cm). Of 18 tumours surrounded by capsule, 14 were invaded the capsule and peripancreatic extension was present in 9 of the cases. Perineural invasion (PNI) was observed 20,8 %(5 of 24) of the patients. There was no peripancreatic spread in 73.7 % of PNI negative patients ($p < 0.05$). Mitotic activity was absent in all cases with one exceptional. One patient died of metastatic disease, 4 months after operation. We observed 10 mitosis/20 HPF, capsule invasion, peripancreatic extension and necrosis in that case. Diffuse and expansive growth, lymphovascular invasion, calcification and cholesterol clefts were also evaluated.

Conclusion: SPN is a low-grade tumour and recurrence or metastasis are not expected. However, 15 % of patients develop metastatic disease. We suggest that perineural and capsule invasion, high mitotic activity and peripancreatic extention could be associated with aggressive behaviour.

PS-07-003

Solitary extramedullary plasmacytoma: An histological turnover on a presumed liver metastasis

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Objective: Solitary extramedullary plasmacytoma (SEP) is a clonal proliferation within non-osseous tissue, representing about 3–5 % of plasma cell dyscrasias. Gastrointestinal-associated SEPs are uncommon, accounting for only 10 % of the cases; liver involvement is exceedingly rare. We describe a case of a patient assumed to feature an hepatic metastatic cancer, which finally heralded a SEP.
Method: An 83 year-old male revealed a 1.8 cm nodule in the right hepatic lobe during imaging follow-up for large-cell neuroendocrine carcinoma (grade 3) of the rectum. Considering the high clinical suspicion for metastasis, no histological evaluation was performed and the patient underwent hepatic segmentectomy.
Results: Grossly, a firm, poorly defined greyish area was recognized, measuring 2.1 cm in greater axis. Microscopically, the lesion consisted of well-differentiated CD56+ plasma cells, exhibiting cytoplasmic restriction for λ light chain. Further investigation failed to disclose marrow plasmacytosis, anemia, hypercalcemia, renal failure, lytic bone lesions or serum M-protein elevation, percluding multiple myeloma (MM).
Conclusion: Extramedullary plasmacytoma in the context of MM indicates advanced disease and portends a poor prognosis, whereas SEP has a generally favorable outcome after local radiotherapy. To our knowledge, this is one of the six cases of hepatic SEP to be reported and the first following a distinct malignancy.

PS-07-004

Liver transplant in HIV patients: A retrospective analysis of twenty-six patients

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Objective: Liver disease is a major cause of mortality and morbidity in HIV patients and so, the number of patients that are HIV positive with chronic liver disease presenting as potential liver transplant (LT) candidates is increasing. Our objective is to review the liver transplants in HIV patients performed at Centro Hospitalar Lisboa Central (CHLC).
Method: We reviewed all the HIV patients that received a liver transplant from 2007 to 2015. Relevant clinicopathological information was collected from clinical files and pathology reports.
Results: Twenty-six HIV positive patients (73 % males and 27 % females) underwent LT. All were orthotopic LT, eight being "domino" transplants from familial amyloid polyneuropathy donors. Twenty were co-infected HIV/hepatitis C virus (HCV), two were co-infected with HIV/hepatitis B virus (HBV), and the other four with multiple co-infections (HIV/HCV/HBV and one with hepatitis delta virus). Twenty-four (92.5 %) showed cirrhosis, with variable activity, and two had also hepatocellular carcinoma. Two (7.5 %) had massive necrosis in the context of acute liver failure of unknown etiology. Twelve (46 %) had post-transplant (PT) liver biopsies, nine (35 %) of which with features of HCV recurrence. One of these was a fibrosing cholestatic hepatitis. A retrospective analysis of these 26 patients showed an overall survival rate of 76,9 %.
Conclusion: Cirrhosis was the main reason that HIV patients performed a LT. Looking at the histology it was clear that the major changes were from virus C infection. The main complication assessed at the PT biopsies was HCV recurrence. Comparing to the literature, PT mortality rate seems similar to HIV negative patients.

PS-07-005

Clinical, pathological and prognostic significance of Beclin-1 expression in hepatocellular carcinoma

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Objective: To investigate the relationship between the expression of beclin-1, an autophagy gene, in HCC with clinical, pathological and prognostic parameters.
Method: This longitudinal study included 155 human liver tissue specimens, 50 from HCC obtained from surgical resection, 50 from adjacent tissue to HCC, 30 liver biopsy sections from hepatitis C virus (HCV), 15 from hepatitis B virus (HBV) and 10 normal liver tissue. Immunohistochemistry of anti beclin-1 antibodiy was performed on tissue microarray of HCC and adjacent tissue whereas liver sections were prepared from the rest of cases. Statistical correlation analyses were performed between beclin-1 expression in HCC and other variables.
Results: Significant alteration in beclin-1 expression in HCC was noticed versus adjacent areas $P = 0.001$, HCV; $P = 0.001$, HBV; $P = 0.01$ and normal liver tissue; $P = 0.001$. Beclin-1 expression in HCC and adjacent tissues was significantly correlated with the degree of differentiation, grade of tumour and non-anatomic resection of tumour. Whereas, beclin-1 expression in HCC revealed non significant correlation with the presence of cirrhosis, vascular invasion, involved margin, the number of focal lesions involved or the histological pattern. Beclin-1 expression was an independent indicator for overall survival in HCC patients ($P < 0.05$).
Conclusion: Beclin-1 may be a valuable prognostic marker for HCC and that regulation of autophagy involves a novel target to currently therapeutic methods.

PS-07-006

Effect of simvastatin on the liver of rats with hyperhomocysteinemia

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Objective: Our objective is to examine the effect of simvastatin on the liver of rats with hyperhomocysteinemia.
Method: Wistar albino rats ($n = 27$; 9/group) were divided into three groups: 1st- ate foods rich in methionine (7,7 g/kg methionine), 2nd- rich in methionine without folate (7,7 g/kg methionine and 0 g/kg of folate, vitamin B6 and B12) 3rd-had a standard diet. All the groups were receiving intraperitoneal simvastatin at a dose of 5 mg/kg body weight. On the liver frozen-section were applied Oil red stain, and on the standard sections HE and Xirius red method. The degree of fibrosis, steatosis, inflammation and the body fat percentage was determined. For statistical processing, SPSS 19.0. was used.
Results: The pronounced steatosis was found in all animals of the first group and in 12.5 % of the animals of the second group. The moderate steatosis was present in 13 % of rats of the second and in 10 % of rats of the third group. Fibrosis was the most significantly present in the second group, but was also present in varying degrees in all groups. No significant difference in the degree of inflammation was observed by the intergroup analysis.

Conclusion: The further study is required that would prove unambiguous therapeutic effect of simvastatin on the liver.

PS-07-007

Ciliated hepatic foregut cyst: Report of four cases and review of the literature

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Objective: Ciliated Hepatic Foregut Cyst(CHFC) is a very rare benign developmental cyst mostly present in adult patients and represents distinctive histopathological features.
Method: We performed a retrospective analysis of four patients with CHFC diagnosed in our department from January 2000 to February 2017.
Results: The patients' ages ranged from 4 months to 12 years. All were females. Two of them were diagnosed antenatally. Three of the cysts located in liver, while one of them was detected in extrahepatic region, adjacent to duodenum. Grossly, cysts were unilocular without any solid areas and measured between 1,5 and 4 cm. Histopathological evaluation of specimens revealed the following: pseudostratified ciliated columnar epithelium, subepithelial connective tissue, smooth muscle layer, and an outer fibrous layer. One of the cysts showed squamous differentiation focally. No mitotic figures were observed in epithelial cells and there was no evidence of pleomorphism or nuclear atypia, suggesting malignancy. Immunohistochemistry for cytokeratin 7 highlighted the origin of the cyst epithelium for all cases. Postoperative courses were uneventful.
Conclusion: CHFC is a quite rare situation accounting for less than hundred cases published and only few of reported in paediatric patients. Because of rarity of this cyst, it is important distunguish it from other cysts such as simple hepatic and choledochal cysts, gallbladder duplication, hydatid cyst, pyogenic abscess.

PS-07-009

Adult pancreatoblastoma, with prominent neuro-endocrine differentiation

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Objective: Pancreatoblastoma is a rare malignant neoplasm, most commonly diagnosed in children, characterized by nests of neoplastic cells with acinar differentiation and distinctive squamoid nests. Neuro-endocrine and ductal differentiation are less common. Herein we present a case of a pancreatoblastoma in an adult patient with prominent neuro-endocrine differentiation.
Method: A 34 year-old male patient with no relevant medical history presented with abdominal pain. Abdominal ecography and CT revealed two hipoecogenic peripancreatic nodules, in the cephalic region, interpreted as lymph nodes. One of the nodules was resected by surgery.
Results: The nodule (2.2 cm) was white and fleshy at the cut surface. By histology, the neoplasm was composed of well defined, highly cellular islands of monotonous cells with ovoid nuclei and evenly distributed chromatin, separated by stromal bands. Nests of epithelioid cells with pale cytoplasm ("squamoid nests") were observed. There was no evidence of lymph node or pancreatic tissue. By immunohistochemistry the neoplastic cells displayed strong expression of sinaptophysin, NSE and CD56, in the absence of expression of trypsin. Nuclear expression of beta-cathenin was observed.
Conclusion: Though extremely rare, pancreatoblastoma can be observed beyond childhood. Neuro-endocrine differentiation is an uncommon feature raising the issue of differential diagnosis with neuro-endocrine tumours of the pancreas.

PS-07-010

A retrospective evaluation of the epithelial changes/lesions and neoplasms of the gallbladder in Turkey and a review of the sampling methods: A multicentre study

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Objective: As there is a continuing issue of disagreement among the observers on the differential diagnosis between the epithelial changes/lesions and neoplasias of the gallbladder, this multicentre study was planned in order to assess the rate of the epithelial gallbladder lesions in Turkey and to propose microscopy and macroscopy protocols.
Method: With the participation of 22 institutions around Turkey which were included in the Hepato-Pancreato-Biliary Study Group, 89,324 cholecystectomy specimens sampled from 2003 to 2016 were retrospectively evaluated. The number of epithelial changes/lesions was identified and the regional and country-wide rate of incidence was presented in percentages.
Results: Epithelial changes/lesions were reported in 6 % of cholecystectomy materials. 7 % was reported as adenocarcinoma, 0.9 % as high grade dysplasia, 4 % as low grade dysplasia, 7.8 % as reactive/regenerative atypia, 1.7 % as neoplastic polyp, 15.6 % as intestinal metaplasia. Remaining lesions (63 %) included primarily non-neoplastic lesions and metaplasias.
Conclusion: The major causes of the difference in reporting of these epithelial changes/lesions and neoplasias include the differences related to the institute's oncological surgery frequency, sampling protocols and differences in the diagnoses of the pathologists. The diagnosis may change if new sections are taken from the specimen when any epithelial abnormality is seen during microscopic examination of the cholecystectomy materials.

PS-07-011

Study of p53 expression in pancreatic ductal adenocarcinoma and its relationship to survival

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Objective: Pancreatic carcinoma is the 4th leading cause of cancer death in western world, with a 5-year survival probability of <10 %. p53 expression as a prognostic marker is under discussion.This study evaluates the IHQ expression of p53 in pancreatic ductal adenocarcinoma and correlates it with patient's response to treatment and survival.
Method: A 50 cases TMA of pancreatic ductal adenocarcinoma and its corresponding negative controls was performed. The p53 positivity degree was quantified establishing 3 categories: no expression; weak expression (<75 %) and intense expression (> 75 %). Survival curves were compared (log-rank test). The degree of significance was 0.05.
Results: Fifty pancreatic ductal adenocarcinomas were studied from 2002 to 2016 (24 male-26 female). 12 patients died in the postoperative period, 18 were p53 negative, 21 showed weak positivity (<75 %) and 11 intense positivity (> = 75 %). 26 % showed histological grade G1, 58 % G2 and 16 % G3. Surgical edge was reached in 16 patients. 33 patients had positive nodes and 5 distance metastases. Weak p53 immunophenotype showed significantly higher progression-free survival (p = 0.03) than those with no expression or intense expression (87 ± 19 months vs 20 ± 6 months).
Conclusion: p53 expression could be helpful to discriminate patients with increased survival prognosis.

PS-07-012

Analysis of pancreaticoduodenectomies from a histopathological perspective - a preliminary study

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Objective: We aimed to examine the histopathological features of patients with pancreaticoduodenectomies (PD).
Method: Records of PDs between 2006 and 2017 were analyzed retrospectively.
Results: There were 279 patients who underwent PD during an 11-year period. The mean age of patients was 60.3 years, with 61.3 % males and 38.7 % females. 243 (87.2 %) patients had malignant, 22 (7.8 %) premalignant and 14 (5 %) benign lesions. According to localisation tumours were divided into ampullary, pancreatic and distal common bile duct. Amongst 135 (55.5 %) cases with ampullary malignant tumours, there were 127 (94 %) adenocarcinomas(AC), 5 (3.7 %) neuroendocrine neoplasms(NN), 1 undifferantiated carcinoma, 1 adenosquamous carcinoma and 1 GIST. Ampullary premalignant lesions were 5 adenomas. Amongst 83 (34.1 %) patients with pancreatic malignant tumour, there were 73 (89.1 %) ACs, 6 (7.2 %) NN, 3 (3.6 %) solid pseudopapillary neoplasms. Pancreatic premalign lesions included 6 intraductal papillary mucinous neoplasms, 6 PanINs, 4 mucinous cystic neoplasms. Distal common bile duct tumours included 23 (92 %) ACs, 2 (8 %) NN, 1 biliary intraepitelial neoplasm in a total of 25 (10.2 %) patients. Benign lesions in ampulla included 2 Brunner gland hyperplasias, 1 duodenitis, 1 ischemia, whereas there were 8 chronic pancreatitis and 1 acinary cell cystadenoma in pancreas and 1 cholangiolithiasis in distal common bile duct.
Conclusion: The present study shows that even though most of the patients are diagnosed with malignancy but pathologists should be aware of the possibility of benign diagnosis in PDs.

PS-07-013

Polypoid endometriosis of the extrahepatic bile duct, mimicking Klatskin tumour

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Objective: Endometriosis is a rare mimicker of malignant extrahepatic biliary tract (EHBT) tumours.
Method: A 43 years old woman, HBsAg carrier for 17 years, presented with sudden sickness. No spesific features were seen on physical examination. MRI suggested a 2,8 cm hypointense mass lesion in hilum, and dilated intrahepatic bile ducts. GGT was 82 IU/L and tumour markers were normal. Preop diagnosis was cholangiocarcinoma. Partial liver resection was performed along with EHBT and gallbladder. Frozen sections for biliary surgical margins were negative for malignancy. On macroscopic examination, common extrahepatic bile duct was compressed by a 2,5 cm polypoid, white mass. Microscopy showed a nodular growth composed of endometrial stroma and glands. The diagnosis was supported by CD10, CK7, ER and PR.
Results: The patient resected for Klatskin tumour diagnosed as polypoid endometriosis on final report. After 7 days in intensive care she died due to liver failure.
Conclusion: Extrapelvic endometriosis is less common than intrapelvic endometriosis. Unusual sites include gastrointestinal and urinary tracts, lungs, nervous system and skin. EHBT location has been described neither in the literature nor in the textbooks and it can be a benign mimicker of Klatskin tumour as seen in this case.

PS-07-014

Microvascular density: Association with tumour volume in pancreatic ductal adenocarcinoma

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Objective: Angiogenesis is a key factor of tumour growth (Weis et al., 2011). It would be an attractive treatment target in pancreatic ductal adenocarcinoma (PDAC), known for its dismal prognosis. As controversies are reported, the study aim was to evaluate microvascular density (MVD) by PDAC size.
Method: In retrospective study of 37 consecutive PDACs, tumour volume (TV) was calculated using ellipsoid formula. Immunohistochemical staining for CD34 was performed. Three most vascularized areas (hotspots) were identified at low power (×40). Microvessels (MV) were counted in three high-power (×200) fields within each hotspot using the manual object count feature of NIS-Elements software. MVD values (MV/mm2) were classified as low (LMVD) versus high (HMVD) according to median MVD (221.1 MV/mm2).
Results: The diameter of evaluated tumours ranged 0.1–6.5 cm, mean 3.3 cm [95 % confidence interval: 2.8–3.7] while TV range was 0.001–67.60 cm3; mean 14.93 cm3 [9.06–20.80]. MVD ranged 121.9–433.7 MV/mm2; mean 237.9 MV/mm2 [210.4–265.5]. Independent t-test showed statistically significant difference by mean TV (but not diameter, grade or localisation) between LMVD and HMVD carcinomas: 9.01 cm3 [6.90–11.12] versus 21.21 cm3 [15.79–26.63]; $p = 0.049$.
Conclusion: In PDAC, higher vascularity is significantly associated with larger TV, implying that a relationship may exist between tumour growth and angiogenesis.

PS-07-016

Correlation of histologic features and genomic landscape in hepatocellular carcinoma

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Objective: To investigate associations between somatic genetic alterations and histologic features in hepatocellular carcinomas (HCC).
Method: Images of diagnostic hematoxylin & eosin (H&E) slides, somatic genetic alterations were retrieved from The Cancer Genome Atlas HCC project. An expert hepatopathologist assessed all H&E slides for histopathologic features, including growth pattern, cytologic variants, the presence of cholestasis or necrosis and Edmondson grade. Associations between the genomic profiles and histologic features were assessed using Fisher's exact tests. $p < 0.05$ were considered significant.
Results: 372/442 cases were classified as bona fide HCCs. Pseudoglanudar HCCs had more frequent CTNNB1 mutations than trabecular/compact HCCs (31 % vs 21 %; $p = 0.043$), while compact HCCs more frequently harbored TP53 mutations than pseudoglandular/trabecular HCCs (42 % vs 21 %; $p < 0.001$). TP53 mutations were also associated with HCCs of Edmondson grade 3/4 (40 % vs 21 % in grade 2; $p < 0.001$) and HCCs with necrosis (44 % vs 26 %; $p < 0.001$). HCCs with cholestasis harbored more CTNNB1 (46 % vs 21 %) and fewer TP53 mutations (15 % vs 35 %; both $p < 0.001$) than those without. HCCs with pleomorphic cells had frequent loss of chr5 and 17p, while high-Edmonson grade tumours had more frequent losses of 1p/4q/16q/17p (TP53)/19p.
Conclusion: Correlation between HCC genetic features and phenotype may further our understanding of HCC biology.

PS-07-017

Pancreatic ductal adenocarcinoma after neoadjuvant therapy: Histomorphologic characterisation

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Objective: Despite the increasing importance of neoadjuvant therapy of pancreatic ductal adenocarcinoma (PDAC), the histomorphology of pre-operatively treated PDAC is poorly characterized, hampering the evaluation of these specimens. We aimed to assess the histomorphological changes in pre-operatively treated PDAC and to determine characteristics that can help distinguish between tumour regression and desmoplasia.
Method: PDAC resection specimens from 27 patients after pre-operative chemotherapy or radiochemotherapy were evaluated. Three tissue samples/patient were selected. Samples were analyzed by alcian blue-PAS and Movat's stain, immunohistochemistry (pan-cytokeratin, alpha-crystallin B, alpha-smooth muscle actin, neurotrophin-3, SPARC, tenascin C, ki-67) and TUNEL apoptosis assay.
Results: Eighty-nine percent of cases were classified as ypT3 or ypT4. Tumour regression according to the College of American Pathologists was 3 (poor) in 4/27 cases (14.8 %), 2 (minimal) in 15/27 cases (55.6 %) and 1 (moderate) in 8/27 cases (29.6 %). Matrix-rich stroma and the expression of alpha-smooth muscle actin and tenascin C ($p = 0.032$) were associated with residual tumour. Tumour regression was associated with lower proliferation index ($p = 0.017$).
Conclusion: PDAC stroma after neoadjuvant therapy is heterogeneous. Movat's stain can help detect sparse residual tumour, which is necessary for tumour regression grading. Although some tested markers are useful indicators, distinguishing between tumour regression and desmoplasia by single markers remains challenging.

PS-07-018

Diagnostic methods of liver fibrosis: A comparison

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Objective: Liver biopsy, previously considered as "gold-standard" method for diagnosing hepatic fibrosis, has been recently challenged by non-invasive diagnostic tools like transient elastography. Our aims were to identify histologic features that correlate with Liver Stiffness (LS) and laboratory-based fibrosis indeces.
Method: Biopsy samples of 96 chronic liver disease patients underwent Digital Morphometric Analysis, assessing the extent and distribution of fibrosis and septal areas. Histologic findings were compared to APRI, HAI (Histologic Activity Index), MetaVIR and LS using Spearman rank-order correlation.
Results: Extent of total and sinusoidal fibrosis showed no correlation with any of the four values. Extent of septal area correlated with each of the four ($p = 0.0016$, Rs = 0.4492; $p = 0.0007$ Rs = 0.4744; $p < 0.0001$ Rs = 0.8446 ; and $p < 0.0001$ Rs = 0.6729, respectively), as well as the amount of fibrosis within the septa and APRI ($p = 0.0087$, Rs = 0.3787), MetaVIR ($p < 0.0001$, Rs = 0.6506), and LS ($p = 0.0002$, Rs = 0.5174), but not with HAI ($p = 0.2326$, Rs = 0.1781).
Conclusion: Liver stiffness showed no significant correlation with total fibrosis of the liver tissue. Although, septal fibrosis correlated with LS, but the best correlation was found with the extent of septal areas, containing both septal fibrotic tissue and adjacent physically deformed hepatocyte cords. Measurements by non-invasive methods correlate well with the histologic appearance of liver fibrosis.

PS-07-020

Can the use of reference pictures improve the interobserver variability on assessment of liver steatosis percentage: A digital platform based approach

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Objective: Liver steatosis percentage (SP) is critical and shows inter/intraobserver variability (IOV) in steatohepatitis diagnosis and donor biopsy assessment. We searched the use of reference pictures, prepared on digital platform, to improve the IOV in liver steatosis.
Method: Twenty pictures of white sphericals with known area measurements, on a pink background was prepared on computer programme, to represent fatty liver microphotographs. Pictures were evaluated by 22 pathologists, and SP were determined twice, first with only pictures, and later with reference pictures showing percentages. The results were compared to computer results.
Results: When compared to the original computer results, SP were high in %70, and same in 19 % in first, 57 % and 32 % in second tour respectively. In the context of steatohepatitis, no whole agreement was seen in first tour and it was 35 % in the second tour. Different grades given were 34 % in first, and 18 % in second. In context of donor biopsy whole agreement increased to 55 % from 35 % with references.
Conclusion: Our study showed that use of reference percentage pictures decreases the IOV, increases true assessment of SP. The study is preliminary to improvement of a digital morphometric steatosis determination system.

PS-07-021

Liver transplantation due to herpetic fulminant hepatitis: A case report

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Objective: Fulminant hepatitis is a common cause of liver transplantation (LT). We describe a case of LT due to herpes simplex virus (HSV) hepatitis in an apparent immunocompetent patient.
Method: .
Results: A 20-year old non-pregnant woman with a known history of deep venous thrombosis in the past, lupus erythematosus and antiphospholipid syndrome was admitted at the Emergency Department (ED) of another institution due to dysuria, urinary urgency, hematuria and painful vulvar ulcers. Her usual medication was warfarin and hydroxychloroquine. At the ED she was given ciprofloxacin and fosfomycin. Five days later she developed fever, nausea, vomiting and back pain. Her blood tests revealed a marked elevation of liver parameters, leucopenia and thrombocytopenia, so that she was transferred to our hospital. The laboratory and clinical situation worsened and she developed liver failure. A LT was performed with a presumed diagnosis of Budd-Chiari syndrome. The histology revealed extensive areas of non-zonal necrosis along with hepatocytes with nuclear enlargement, multinucleation and nuclear inclusions with margination of the chromatin. The immunohistochemistry for HSV2 was positive.
Conclusion: HSV infection is a rare but possible cause of fulminant hepatitis. In some instances LT may be the only option to these patients.

PS-07-023

Synchronous intraductal papillary mucinous neoplasm (IPMN) and serous cystadenoma in the body of the pancreas

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Objective: Intraductal papillary mucinous neoplasms (IPMNs) and serous cystadenomas (SC) are well known cystic neoplasms of the pancreas. However, the simultaneous presentation of both within a neoplasm is very rare.
Method: .
Results: A 77 year-old female with a past history of breast cancer, radiation pneumonitis, dislipidemia and bilateral hipoacusia was diagnosed with a multiloculated cystic lesion in the body of the pancreas measuring 3,6 cm. The endoscopy showed features suggestive of both IPMN and SC. The cyst fluid had elevated CEA and amylase levels and the cytology showed mucus and epithelial cells with mild atypia. A distal pancreatectomy was performed. Histology revealed a cystic lesion composed of areas of a low grade gastric IPMN and others of SC. The cystic spaces were intermingled but each one had only one type of cells. No invasive component was present.
Conclusion: Synchronous presentation of IPMN and SC within a cystic neoplasm is very unusual with just a few case reports in the literature. Awareness of this possibility may be important for the correct interpretation of imagiologic and cytologic findings.

PS-07-024

EMT in anaplastic component of the pancreatic ductal adenocarcinoma

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Objective: EMT represents conversion of an epithelial cell in an elongated cell with mesenchymal phenotype, which can occur in physiologic and pathologic processes. In malignant tumours, EMT-related invasion and migration of tumour cells in blood flow is associated with poor prognosis, high metastatic rate, and low disease-free survival time.
Method: The objective of our study is to detect the epithelium-mesenchyme transformation in AC of PDAC based on IHC.
Results: AC was found in 25/100 of PDAC. It has characterized as a big polymorphic or spindle cells with hyperchromic nuclei, sometimes it was polynucleic cells with minimal stromal component. The volume of AC was ranged from 5 to 20 % of total tumour volume, but in all cases was not predominant. In AC we've found diffuse expression of vimentin and CK7 in some cells. Expression E-cadherin was negative in AC in contradistinction to N-cadherin, which was positive in some cells of AC. The PDAC with AC has had often R1-resection, extraPn1, but rare LNs1-status.
Conclusion: in this study we have found, that cells of AC present only mesenchymal phenotype (complete EMT), whereas cells glandular component display a dual epithelial-mesenchymal expression, also known as an amphicrine pattern. Mesenchymal phenotype promotes direct growth of the tumour in the duodenum, perineural invasion, peripancreatic tissue and R1-status, that development of locoregional recurrence in patients with PDAC. This is what necessitates a combined approach to the treatment of these patients, including surgery, supplemented by conducting IORT that effectively influences on tissues and reduces the number of local recurrence.

PS-07-025

Clinicopathological study of intra-patient inter-tumoural heterogeneity in colorectal liver metastasis

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Objective: We performed a clinicopathological study in patients undergoing hepatectomy for colorectal liver metastasis (CRLM) with/without preoperative treatment to investigate the relationship of intra-patient inter-tumoural heterogeneity with the outcome.
Method: Patients undergoing liver resection for CRLM from 2005 to 2013 were investigated (143 patients with 403 lesions), including patients untreated (19 patients with 29 lesions) and treated with chemotherapy alone (33 patients with 91 lesions), chemotherapy with anti-VEGFR (47 patients with 157 lesions), and chemotherapy with anti-EGFR (44 patients with 126 lesions). All specimens were reviewed to assess tumour regression grading (TRG), histological growth pattern (HGP), and chemotherapy-related liver injuries.
Results: Multivariate analysis showed that worst TRG, sinusoidal obstruction syndrome (SOS) and steatohepatitis were significant predictors of a shorter progression free survival (PFS). Desmoplastic HGP was a significant favorable predictor for PFS and overall survival (OS). Among multiple lesions cases ($n = 83$), intra-patient inter-tumoural heterogeneity was defined by the variation of the TRG score: (i) a homogeneous group composed of patients with lesions belonging to either low (1–2) or high TRG (3–5) or (ii) a heterogeneous group composed of patients with lesions belonging to different TRG categories. The heterogeneous group had a shorter PFS and OS.
Conclusion: Intra-patient inter-tumoural heterogeneity, steatohepatitis, and SOS are crucial prognostic factors.

PS-07-026

Ki67 utility in the diagnosis, prognosis and management of pancreatic ductal adenocarcinoma

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Objective: The most important prognostic factors in Pancreatic Ductal Adenocarcinoma (PDA) are stage and surgical margin involvement (SMI). Assessment of SMI in ADP resection specimen on chronic pancreatitis (CP) is challenging, being difficult discerning between ductal reactive proliferation (ADM) and ADP. The objective was to determine usefulness of Ki67 when assessing SMI and its prognostic value in ADP.
Method: Ki67 was evaluated in 64 ADP and 15 ADM of CP, determined by immunohistochemistry. Association of Ki67 with clinicopathological parameters, overall survival (OS) and disease-free survival (DFS) was statistically analyzed. ROC curve analysis was performed.
Results: We observed significant association between stage and worse OS; SMI and worse survivals. Study of Ki67 demonstrated significant association with high grade tumour differentiation, without signification with prognostic value parameter, KRAS mutation or survivals. Statistically significant difference in Ki67 expression was observed between ADM of PC and ADP (cutoff point ≥20; positive predictive value (PPV) of 100 %).
Conclusion: Ki67 is a technique available in all pathology laboratories, reproducible and easy to implant in clinical practice. Ki67 ≥ 20 allows distinguishing between MAD and ADP (PPV:100 %). Ki67 determination may be useful assessing small pancreatic biopsies with loss of architectural orientation and in determining SMI of ADP resection specimen on CP.

PS-07-028

ALK expression in intrahepatic cholangiocarcinoma

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Objective: ALK traslocations are involved in several types of cancers. Nevethrless,only in anaplastic lymphoma and non-small cell lung adenocarcinoma ALK aberrations are well investigated with

clinical application. The aim of this study was to evaluate the frequency of ALK expression in intrahepatic cholangiocarcinoma (CCC) using IHC and FISH.
Method: One study group included 33 patients with CCC diagnosed and operated over period of 5 years (2010–2015). Men - 15, women- 18, median of age (67, ranges 58–82). IHC was performed and evaluated. In situ hybridisation was performed in positive IHC-cases.
Results: Weak-positive ALK expression was found by means of IHC in 3 cases (9,1 %). Fluorescence in-situ hybridisation revealed no ALK traslocations in all 3 cases.
Conclusion: ALK translocation was not found in our group of patients with CCC. Immunohistichemical expression in 3 cases (9,1 %) may be reflected by and associated with some other ALK abberations of this gene (not translocations!). Further investigations with more numberous groups of patients are required.

PS-07-030
Comparison of Sonic Hedgehog and keratin 8/18 immunostains as markers of ballooned hepatocytes in non-alcoholic fatty liver disease (NAFLD)
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Objective: Hepatocyte ballooning is required for the histological diagnosis of non-alcoholic steatohepatitis (NASH). Identification of ballooned hepatocytes (BH) is hampered by high inter-observer variability. Absence of keratin 8/18 (K8/18) and presence of Sonic hedgehog (Shh) cytoplasmic immunostain have been proposed as BH markers but their utility in clinical practice has not been assessed.
Method: Serial sections of needle liver biopsies with NAFLD from 74 patients (M/F 39/35, mean age 47.9 [21–73] years) were immunostained for Shh (ab53281, Abcam, USA) and K8/18 (K8 Ab-8, K18 Ab-1, NeoMarkers, USA). The number of Shh-positive or K8/18-negative cells, isolated or in groups, was counted.
Results: Simple NAFLD and NASH (stage 0 $n = 4$, 1 $n = 15$, 2 $n = 14$, 3 $n = 8$, 4 $n = 6$) were diagnosed in 27/74(36.5 %) and 47/74(63.5 %) cases, respectively. Shh immunostain highlighted more BH (6.67 ± 9.46) compared to K8/18 (3.26 ± 6.23) per NASH biopsy. Shh detected more BH than K8/18 in 20/47(42.6 %), less BH in 8(17 %) and equal numbers in 19 (40.4) NASH biopsies.
Conclusion: K8/18 and Shh are useful markers for the objective assessment of BH in liver biopsies of NAFLD patients. Shh is more sensitive than K8/18 immunostain in detecting BH in NAFLD and its use may aid the histological diagnosis of NASH.

PS-07-031
High-grade intraepithelial lesions are helpful for identifying origin of periampullary cancers
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Objective: Recognition of accurate origin of periampullary cancers is important because of different clinicopathologic behaviors based on their origin. The presence of intraepithelial precursor lesions, including high-grade pancreatic intraepithelial neoplasias (PanINs) or and biliary intraepithelial neoplasias (BilINs) may suggest origin of the periampullary carcinomas in challenging cases.
Method: To prove utilities of high-grade intraepithelial precursor lesions for identifying origin of ambiguous periampullary cancers, status and grades of PanINs and BilINs were evaluated from 257 consecutive pylorus-preserving pancreaticoduodenectomy specimens with well-defined cancer origin, including 114 pancreatic cancers, 82 distal bile duct cancers, 54 ampullary cancers, and 7 duodenal cancers.
Results: High-grade PanINs were more commonly noted in pancreas cancers (21.9 %, 25/114) than distal bile duct (8.5 %, 7/82), ampullary (9.3 %, 5/54), and duodenal (0 %, 0/7) cancers ($p = 0.02$). Similarly, high-grade BilINs were more frequently identified in distal bile duct cancers (56.1 %, 46/82) than ampullary (24.1 %, 13/54), pancreas (9.6 %, 11/114), and duodenal (0 %, 0/7) cancers ($p < 0.001$).
Conclusion: High grade PanINs were most commonly noted in pancreatic cancer, while high-grade BilINs were most frequently seen in distal bile duct cancer. Recognition of high-grade intraepithelial lesions will be helpful for identifying primary origin of periampullary cancers, especially when epicenter of periampullary cancer may be ambiguous.

PS-07-033
Kaposi sarcoma of the liver in post renal transplantation
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Objective: Kaposi sarcoma (KS) of the liver is rarely reported and is incidentally discovered on imaging or autopsy examination primarily in HIV-related conditions. However, it is exceedingly rare in other immunocompromised conditions as in solid organ transplantation. In such cases, it is considered as a de novo malignancy. We report a case of hepatic KS in a post-renal transplant patient.
Method: A 34-year-old and HIV-negative male, with a past medical history of Alport syndrome and renal transplantation, presented with hypervascular hepatic, pancreatic and pulmonary nodules discovered by imaging performed for routine follow-up. A pancreatic neuroendocrine tumour with visceral metastases was suspected. A subsequent needle liver biopsy was performed.
Results: Histologically, the liver parenchyma displayed a spindle cell proliferation that formed slit-like spaces with extravasation of erythrocytes and hemosiderin deposits. The tumour cells infiltrated portal tracts with a growth into sinusoidal spaces. On immunohistochemistry, tumours cells were positive for human herpes virus 8 (HHV8).
Conclusion: Liver is an unusual site of KS in the non-HIV population. Its true incidence is not well-documented but seems to be higher in Africa. In post-transplant recipients, it is a de novo virally induced malignancy and direct oncogenic effects of immunosuppressive therapy is the main mechanism of pathogenesis.

PS-07-034
Neonatal congenital pancreatic cyst: A report of four cases
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Objective: Neonatal congenital pancreatic cyst (NCPC) is rare with an incidence less than 1 % of all abdominal cysts. We report four cases of NCPC with a review of the literature.
Method: Four cases of NCPC were diagnosed in the department of pathology of Monastir Hospital between 2010 and 2016. Data were collected from medical files.
Results: Four full-term infants (3 females and 1 male) aged between 1 and 120 days presented with abdominal cystic malformation. Diagnosis was prenatal in two patients. Radiologic findings indicated the pancreatic origin of the cysts. These cysts were associated to Ivemark syndrome in two cases and solitary in the other cases. Surgical resection was performed. Cyst punction drew out a yellowish liquid with high amylase and lipase levels. Macroscopically, cysts measured between 3.5 and

10 cm. Histologically, the cystic wall was lined by a bi or mono-stratified cubic epithelium and it was prolonged by a normal pancreatic tissue. Liver biopsy concluded to secondary biliary cirrhosis in two cases.
Conclusion: CPC in paediatric population are very rare. Embryologically, this cyst occurs as a result of sequestration of pancreatic ducts. Early diagnosis is important to prevent complications. Prognosis is dependent on early management and on associated malformations.

PS-07-036
Primary hydatid cyst of the pancreas: A case report
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Objective: Hydatid disease can involve any organ of body but primary pancreatic involvement (without liver or lung disease) is extremely rare with an incidence of 0.1–2 % of hydatid disease.
Method: A 36-year old female patient was admitted to our surgery outpatient clinic with the epigastric pain. Magnetic resonance imaging demonstrated a multilocular cystic lesion sized 55 × 50 mm in the tail of the pancreas but the pancreatic duct was not dilated. The patient underwent distal pancreatectomy.
Results: Macroscopic examination of the surgical specimen showed a 6.5 cm multilocular grey-yellow cystic lesion with thick wall and multiple fluid filled vesicels. Histologic examination of the cyst wall revealed that its was composed of a germinative membrane, cuticular layer, fibrous capsules and its lumen contained daughter vesicles. The histopathologic diagnosis was reported as a hydatid cyst.
Conclusion: Preoperative diagnosis of pancreatic hydatid cyst is diffucult as its radiologic findings are often mistaken for pseudocysts, cystadenocarcinoma, and congenital or post-traumatic cysts. So it should be included in the differential diagnosis of cystic lesions and cystic malignancies of the pancreas.

PS-07-037
Pancreatic neoplasm with triple neuroendocrine ductal and acinar cell differentiation: A case report
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Objective: Mixed neuroendocrine-nonneuroendocrine neoplasms of the pancreas (MiNEN) are very rare and defined by at least 30 % of any component of the lesion. We present a case of MiNEN with uncertain malignant potential.
Method: In a 49-yrs old female patient who suffered abdominal discomfort, ultrasound and preoperative CT scan imaging revealed solid mass in the pancreatic body. There were no other significant or conclusive laboratory findings. Routine histopathological and immunohistochemical examinations were performed on resection specimen of distal pancreatectomy.
Results: Gross examination revealed sharply circumscribed pancreatic tumour, measuring 26 mm in greatest diameter. Histomorphology exhibited well differentiated triphasic proliferation with intermingled components of dominant neuroendocrine and accompanying nonneuroendocrine (ductal and acinar) components. Immunostaining of neuroendocrine component expressed somatostatin, proinsulin and glucagon positivity in about 60 , 20 and 5 % tumour cells, respectively; CK7 and CK19 were positive only in ductal and Bcl-10 only in acinar component, but trypsin was expressed also in some ductules. Proliferation Ki-67 index was estimated about 1 % and mitotic activity was 1/10 HPF.
Conclusion: MiNEN with three components is exceptionally rare and should be considered in the differential diagnosis. We also assumed reactive atypical ductal proliferation with acinar cell metaplasia in well differentiated pancreatic neuroendocrine tumour.

PS-07-038
The possibility of TGF-beta activation by macrophage and/or neutrophil in NASH pathogenesis
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Objective: In NASH (nonalcoholic steatohepatitis) pathogenesis, TGF-beta plays a pivotal role in hepatic fibrosis. It is considered that TGF-beta is produced as an inactive latent complex, in which active TGF-beta is enveloped by its pro-peptide, the latency-associated protein (LAP), and PLK (plasma kallikrein) activates TGF-beta by cleavage between R58 and L59 residues within LAP, and the N-terminal side LAP degradation products ending at residue R58 (R58 LAP-DPs) functions as a footprint of PLK-dependent TGF-beta activation. Regulating TGF-beta activation could have possibilities of inhibiting hepatic fibrosis. In order to control TGF-beta activation, it is necessary to identify the local place (tissue and/or cell) where fibrosis occurs. Thus, we focus on the localisation of TGF-beta R58 LAP-DP in NASH fibrosis mouse models.
Method: We've performed histocytochemical analysis with R58 LAP-DP specific mouse monoclonal antibody for immunohistocytochemistry by means of LM and TEM in NASH models (MC4R KO mice, CDAHFD mice, and FLS-ob/ob mice), and human.
Results: We found that the R58 LAP-DPs were localized around the lipid droplets in NASH liver, especially macrophage and inflammatory cells.
Conclusion: These findings insisted that macrophage and inflammatory cells were involved TGF-beta activation causing fibrotic disorder, and the possible inhibition of hepatic fibrosis could be achieved by regulating those cells function.

PS-07-039
Ciliated hepatic foregut cyst
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Objective: Ciliated hepatic foregut cysts are typically benign, rare, embryological epithelial cysts of the liver and usually asympthomatic. There are 103 cases only 10 of which relate to children in the English literature.
Method: 15-month- old male patient presented with a hemangioma on his left arm. Due to the suspicion of an additional intrabdominal pathology, an abdominal ultrasonography was performed. Incidentally, a smooth bordered cystic lesion sized 45 × 45 mm in the right lobe of the liver was found. Magnetic resonance cholangiopancreatography showed the dilatation of the intrahepatic bile ducts next to the cyst. The cyst was surgically resected and macroscopically the specimen was a thin fragmented cyst wall measuring 55 × 15 × 10 mm. The cyst had a smooth lining without any papillary projections. Histopathologically unilocular cyst with ciliated epithelial lining surrounded by smooth muscle and loose connective tissue was detected.
Results: The final diagnosis was ciliated hepatic foregut cyst.
Conclusion: Hereby, we present a rare case of a ciliated hepatic foregut cyst in a paediatric patient with a rare localisation (right lobe of the liver) by discussing the differential diagnosis including simple cysts, parasitic cysts, intrahepatic choledochal cyst, cystic mesenchymal hamartoma, and cystic malignant tumours.

PS-07-040
KRAS mutations are predominant in Non-mucinous Lining Epithelia (NMLE) of pancreatic Mucinous Cystic Neoplasms (MCNs)
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Objective: MCNs of the pancreas are cystic neoplasms with mucinous lining epithelia (MLE) and ovarian-type stroma. Although NMLE are

observed in some MCNs, debates exist whether cystic tumours with NMLE considered as MCNs or different disease entity.
Method: NMLE was defined as flat or cuboidal biliary epithelial cells without containing mucin. 102 MCNs were classified as MCNs with NMLE and MCNs with MLE. Twelve MCNs with NMLE were selected for KRAS mutational analyses with droplet digital PCR after LASER captured microdissection.
Results: Patients were 110 females and 2 males with mean age of 46.5 ± 12.3 years. NMLE was noted in 76.8 % (86/112) of MCNs with 46 % of epithelia. MCNs with diffuse (>50 %) NMLE were 38.4 % (43/112), and smaller (4.2 ± 2.1 cm) than tumours with MLE (6.0 ± 3.6 cm, $p < 0.01$), and all were low grade without accompanying high grade/carcinoma in situ. KRAS mutation was detected in 92 % (11/12 cases) of NMLE. Among 9 MCNs with matched MLE and NMLE, 7 had KRAS mutations both in MLE and NMLE ($p = 0.34$).
Conclusion: Diffuse NMLE are common in MCNs with small size and low grade dysplasia. Frequent KRAS mutations are observed both in NMLE and MLE. Therefore NMLE with MCNs are the same disease entity with MCNs.

PS-07-041
Carcinosarcoma of the gallbladder: A case review
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Objective: Carcinosarcoma of the gallbladder is very rare primary tumour having distinctive histomorphological and immunohistochemical features. However, besides similarities with gynecological type of carcinosarcomas, it represents problematic issue for correct diagnosis and treatment.
Method: We present a case of large epigastric mass in a 71-yrs old male patient who suffered right upper quadrant abdominal pain. Preoperative MDCT-scan was interpreted as (peri)gastric and/or (peri)hepatic mass involving IVb segment, leading to radical surgery. Follow-up of histopathologically diagnosed carcinosarcoma after 10 months revealed unresectable hepatic metastases and we were asked to perform Her-2 testing for possible therapeutic treatment.
Results: Gross examination revealed circumscribed cystic tumour of the gallbladder with dominant extramural and intrahepatic growth, measuring 140 mm in greatest diameter. Histology exhibited biphasic tumour with intermingled adenocarcinomatous and atypical mesenchymal components (mitotic activity 4/10 HPF) with large chondrosarcomatous areas. Immunostaining of epithelial component showed strong HER-2, COX2, EGFR and androgen receptor positivity in about 60 , 70 , 20 and 95 % tumour cells, respectively. To date we have no results of oncologic treatment.
Conclusion: Carcinosarcoma with chondrosarcomatous component is rare histological presentation of the gallbladder that broadens differential diagnosis. Immunoexpression of HER-2 and other predictors might be helpful in planning further appropriate treatment.

PS-07-042
A correlation between Glypican-3 (GPC3) expression and the grading system in hepatocellular carcinoma
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Objective: Primary hepatocellular carcinoma (HCC) is a malignant proliferation with hepatocellular differentiation, the most frequent primary liver malignancy and the 5th most common malignancy worldwide. The purpose of this study was to determine the variability of GPC3 expression in hepatocellular carcinomas based on the Edmondson-Steiner grading system.
Method: Grading of hepatocellular carcinoma is based on the Edmondson—Steiner system, on a scale from grade 1 (well differentiated) to grade 4 (undifferentiated). HCC Grade 1 has a trabecular pattern similar to normal hepatocytes, whereas Grade 4 HCC often has a solid (compact) architecture, with a high degree of pleomorphism. We studied the imunophenotypic profile of 27 cases diagnosed in our pathology department as hepatocellular carcinomas, in the last 12 months. Five cases were diagnosed as Grade I/II (18.52 %), 20 cases as Grade II/III (74.08 %) and 2 cases as Grade III/IV (7.40 %) Edmondson-Steiner.
Results: Diffuse cytoplasmic and membranous staining for GPC 3 was registered gradually with the highest intensity documented in Grade II/III Edmondson-Steiner HCC and the lowest intensity in Grade III/IV Edmonson-Steiner HCC.
Conclusion: GPC3 is a useful marker for establishing the grading of hepatocellular carcinomas in correlation with the Edmondson-Steiner classification.

Monday, 4 September 2017, 09:30–10:30, Hall 3
PS-08 Haematopathology

PS-08-001
Crossing paths with lymphomas: A difficult case of histopathological diagnosis
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Objective: What initially appeared to be a simple case of lymphoma originating from the colon turned out to be more than meets the eye
Method: We report the case of a 51 year old woman who underwent splenectomy after a traumatizing accident which occurred 2 years ago. Following a routine checkup in late 2016, a tumour-like mass is discovered at the junction between the sigmoid and the descending colon. Frozen examination raised the suspicion of angioimmunoblastic lymphoma
Results: Histopathological examination infirmed the initial diagnosis and raised the suspicion of Castleman's disease based on abnormal vascularity and regression of germinal centers. Under closer examination, the pseudotumoural mass was resembling spleen tissue. Immunostaining for CD8 and CD34 was necessary for differential diagnosis and both stains were positive. It is noteworthy that the only positive endothelial cells for CD8 are the spleen littoral cells. Thus, we established the final diagnosis of splenosis.
Conclusion: This case sets the stage for a discussion regarding the way the human body acts to regenerate pieces of pertaining to the self that are missing. The pathological approach was also one that posed a great deal of wonder to the case, since growth of tissue with the same function of an excised organ is quite uncommon.

PS-08-002
Small cell variant ALK positive anaplastic large-cell lymphoma presenting as an endobronchial mass in a patient with synchronous breast carcinoma
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Objective: Small cell variant ALK positive anaplastic large-cell lymphoma (SCVALK + ALCL) is uncommon. Endobronchial involvement by ALCL is exceedingly rare.
Method: We present a case of SCVALK + ALCL presenting as an endobronchial mass in a patient with synchronous no special type (NST) breast carcinoma.
Results: A 63 year-old woman with irrelevant past history presented with recurrent respiratory infections treated with antibiotics. Chest CT displayed a peribronchial consolidation in right lung.

Bronchofibroscopy showed an endobronchial mass in the middle bronchus that was biopsied. The biopsy displayed a bronchial mucosa occupied by "atypical" lymphoid cells with irregular nuclei and scant cytoplasm growing diffusely. Scattered "hallmark" cells were identified. The "atypical" cells were positive for CD30, ALK and EMA and negative for CD45, CD3, CD20, granzyme and perforin. A diagnosis of small cell variant ALK positive anaplastic large-cell lymphoma null-phenotype was performed. During staging for lymphoma, a PET/CT showed metabolically active disease in the right middle bronchus, left supraclavicular, mesenteric and paraaortic lymph nodes and in a suspicious breast nodule. Microbiopsy of the nodule showed grade II NST breast carcinoma.
Conclusion: Although rare, ALK + ALCL should be considered in the diagnosis of endobronchial tumours. The detection of an unrelated neoplasia during staging procedures is a possibility, particularly in older patients.

PS-08-003
Lymph node core biopsy: 15 years of lymphoma diagnosis in a tertiary institution
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Objective: The diagnosis of lymphoma relies on lymph node/extranodal excisional biopsy as a gold standard procedure. However, core needle biopsies (CNBs) have been progressively established as an alternative tool, allowing to bypass logistical intricacies, inflated costs and various procedural risks, while delivering a majority of diagnostic samples. Herein, we present our 15 year-long experience under this approach.
Method: Reports of lymph node CNBs concerning the 2002–2016 period were retrospectively assessed for age, size and pathology; samples presenting lymphoma were further classified regarding the extent/confidence of their diagnosis and bisected according to the ability to prompt treatment.
Results: A total of 495 reports were reviewed, encompassing 469 patients from 9 to 94 years old and samples from <1 to 40 mm; 17 % were deemed insufficient/inadequate, 18 % fell into the unspecific/lymphadenitis scope, 31 % revealed metastatic neoplasia and 34 % displayed lymphoma. Regarding the latter, 72 % were fully diagnostic, 22 % partially diagnostic (unfit to reach a subclassification) and 6 % equivocal (unsuited to ascertain the presence of lymphoma); 93 % of the samples were regarded as actionable.
Conclusion: Despite our higher rate of actionable diagnoses (93 % versus 74 %), this series is in accordance with previous studies, which reported a formal lymphoma diagnosis in 82–97 %, highlighting the method efficiency.

PS-08-004
Quality improvement in determining genetic alterations in the diagnosis of "double-hit" B-cell lymphomas
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Objective: To investigate the accuracy of IQ-FISH (fluorescent in situ hybridization) to improve the response time for FISH evaluation in high grade B-cell lymphoma.
Method: Between July 2016 and February 2017 we prospectively analysed 27 cases of "de novo" diffuse large B-cell lymphoma (DLBCL) for MYC, BCL2 and BCL6 rearrangements using in parallel our conventional Vysis probes and the IQ-FISH probes. Cases were selected on a morphological basis based on diffuse growth pattern and cell size; the only excluding criteria was relapse/transformation from a previous lymphoma. We evaluated the response time as the time from the H&E stained slide to the moment we got the FISH result.
Results: Of the 27 cases analysed 22 were diagnosed as DLBCL. 4 out of 20 evaluable cases showed MYC rearrangement, 2/21 BCL2 rearrangement and 4/21 BCL6 rearrangement with IQFISH-probes; 2/20 (10 %) cases were double hit lymphomas showing MYC and Bcl-2 rearrangement. The correlation between the two FISH methods was 93,6 %, and the diagnostic correlation is 90 %. Median response time was 1,4 days for IQFISH-probes and 5,9 days for conventional FISH-probes.
Conclusion: IQFISH results can improve the response time in the diagnosis of High grade and "double-hit" B –cell lymphomas.

PS-08-005
Composite lymphoma: An improbable diagnosis in core needle biopsy
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Objective: Composite lymphoma is a rare entity defined as the synchronous co-existence of two or more distinct lymphomas within the same tissue; it is customarily described in excised specimens. Throughout the past 7 years we diagnosed 3 cases in core needle biopsy (CNB) samples.
Method: Case 1: a 70 year-old woman with a 3-year history of multiple myeloma (MM) was submitted to a follow-up osteomedullary CNB. Case 2: a 70 year-old man with lymphocytic lymphoma/chronic lymphocytic leukaemia (LL/CLL) diagnosed 19 years before with signs of progression that underwent an osteomedullary CNB. Case 3: a 65 year-old woman without previous history of haematological malignancies presented with a retroperitoneal mass which was biopsied. CNBs were studied using H&E and immunohistochemical techniques.
Results: Case 1 was diagnosed as MM and small B-cell non-Hodgkin lymphoma; the splenectomy specimen later unveiled a splenic marginal zone lymphoma. Case 2 was reported as LL/CLL and Hodgkin lymphoma (HL), both later confirmed in an excised lymph node. Case 3 consisted in follicular lymphoma and HL which showed remission after treatment, tackling fatal outcome thus far.
Conclusion: Diagnosing composite lymphomas in CNB is a challenging—but feasible—task. To our knowledge this is the first series of composite lymphomas diagnosed through CNB.

PS-08-006
Simultaneous occurence of peripheral t cell lymphoma with follicular helper phenotype and chronic lymphocytic leukemia/small cell lymphoma like B cell infiltration
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Objective: Chronic lymphocytic leukemia/small lymphocytic lymphoma(CLL/SLL) is relatively common and patients occasionally develop other neoplasms; however patients who develop other types of lymphomas are rare. Here in we report a case with simultaneous occurance of peripheral T cell lymphoma (PTCL) and CLL/SLL like B cell infiltration.
Method: Bone marrow, liver and paravertebral mass biopsies were evaluated. Immunohistochemistry was performed to all three formaline fixed parafine embedded tissue samples.
Results: A previously healthy 63-year-old man presented with fever, weight loss and night sweats. Laboratory findings revealed increased LDH, ALP, GGT as well as pancytopenia. Bone marrow biopsy revealed composite lymphoma. First component was consistent with CLL/SLL like B cell infiltration and the second component was consistent with PTCL with T follicular helper(TFH) phenotype. Furthermore a focus of hemophagocytic activity was observed. PET-CT study revealed left paravertebral mass at cervical region. Paravertebral mass and liver biopsy showed PTCL with TFH phenotype and CLL/SLL like B cell infiltration, respectively.

Conclusion: Composite lymphomas containing both T and B cell lymphomas are very rare. Moreover, synchronous cooccurence in the bone marrow and accompanying hemofagocyte activation is an exceptional event of which is probably related with immune dysregulation.

PS-08-007

Hodgkin's lymphoma with aberrant T-cell expression: A diagnostic challenge

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Objective: Hodgkins lymphoma with aberrant T cell expression, comprises less than 5 % of all Hodgkins Lymphomas with less than 2 % Reed Sternberg cells expressing two T lineage markers with the commonest being CD2 and rarest being CD8. Here we present a case which posed a major diagnostic challenge.
Method: A 26 year female presented with fever and generalized lymphadenopathy. A biopsy of the left axillary lymph node was done. Immunohistochemistry and additional molecular tests were done to confirm the diagnosis.
Results: The biopsy revealed lymph node with effaced architecture showing large areas of necrosis along with atypical cells containing prominent nucleoli. These cells were strongly positive for MUM1, and focally positive for PAX5, CD15 and CD30. Expression of CD2 and CD8 was also noted. A panel of other T cell markers, ALK and EMA was done. T-Cell Rearrangement and EBER in situ hybridization was performed to clinch the diagnosis
Conclusion: Hodgkins lymphoma with aberrant T cell expression can be misdiagnosed as T cell lymphomas with aberrant B cell expression. This distinction is important as it has both therapeutic and prognostic significance. Patients have a reduced overall survival and poor prognosis in cases of Hodgkins with aberrant T cell expression as compared to classical HL.

PS-08-008

Characteristic of the bone marrow morphological criteria, Cyclin D1, p53 expressions and that correlation with different stages and ß-2 microglobulin level of patient with multiple myeloma

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Objective: The bone marrow (BM) biopsies in patients with multiple myeloma (MM) are usually analyzed by some morphological criteria and aberrant markers- p53, Cyclin D1 which can help to predict its prognosis (Bartl; Subramanian; Athanasiou)
Method: We have analyzed 122 patients with primary diagnosed MM from years 2011 to 2015
Results: We proved that increased beta-2 microglobulin (β-2 MG) level statistically significantly correlated with increased BM cellularity ($p < 0.0001; r = +0.45$), increased plasma cells (PC) in BM ($p < 0.0001; r = +0.47$), high level of PC with plasmablastic differentiation ($p = 0.0001; r = +0.34$), the BM infiltration type with PC ($p < 0.0001$; $r = +0.43$), overexpression of p53 ($p = 0.0025; r = +0.27$) and Cyclin D1 ($p = 0{,}033; r = +0{,}19$). Statistically significant associations were found between MM advanced Salmon-Duri (SD) clinical stage and increased BM cellularity ($p < 0.0001$; $r = +0.4$), increased amount of PC ($p < 0.0001; r = +0.5$), high number plasmablastic differentiation of MM cells, BM infiltration type of PC ($p < 0.0001; r = +0.44$)) as well as with Cyclin D1($p = 0{,}002; r = +0.28$) and p53 ($p < 0.0001; r = +0.41$) overexpression
Conclusion: High BM cellularity and increased PC level, as well as high number of PC with plasmablastic differentiation, diffuse type infiltration of PC and Cyclin D1, p53 overexpression in PC significantly correlated with advanced SD stages and high beta-2microglobulin level and are linked to poorer prognosis of MM cases.

PS-08-009

Extramedullary blast crisis in a patient with chronic myelogenous leukemia: Testicular involvement with mixed B lymphoid/myeloid phenotype

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Objective: Blast phase in chronic myelogenous leukemia (CML) has rarely been reported to involve extramedullary sites. We present a particular case of this condition in a 20 years old male with extramedullary biphenotypic blast crisis (B lymphoid/myeloid) involving the testicle
Method: A 20 years old male was admitted to hospital with testicular tumour in 2014. He was a known case of CML diagnosed in 2013 and under ongoing treatment with Imatinib. Histopathological and immunohistochemical examinations of the testicular biopsy specimen were performed, along with cytogenetic and molecular assessments.
Results: The histopathological evaluation revealed a diffuse neoplastic infiltrate composed of blasts cells. Immunohistochemical examination disclosed the immature cells to coexpress both B surface lymphoid blasts antigens (CD20, CD79a, CD10, PAX5, TdT, CD34) and myeloid antigens (CD117, MPO). Bone marrow aspiration showed absence of blast cells and normal cytogenetics. BCR-ABL/ABL (Breakpoint cluster region-Abelson) ratio was 0,452 % in peripheral blood and 0,244 % in bone marrow.
Conclusion: The histopathological, immunophenotypic, molecular and cytogenetical findings supported the diagnosis of testicular involvement in biphenotypic blast crisis (B lymphoid/myeloid) of CML. To our knowledge, only six cases of CML blast crisis affecting the testicle have been reported so far, however none of them had a mixed B lymphoid/myeloid phenotype.

PS-08-010

EBV positive diffuse large B cell lymphoma: Evaluation of 29 cases with morphologic and immunohistochemical features of a rare entity

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Objective: Epstein-Barr virus (EBV) positive diffuse large B-cell lymphoma (DLBCL) of the elderly had been included in the 2008 WHO classification as a new provisional entity, but since then it has been increasingly recognized in younger patients. Therefore, this entity has been modified in the 2016 revision of the WHO classification as a real entity and termed as "EBV positive DLBCL, NOS".
Method: A total of 29 cases, diagnosed between 2000 and 2016, were retrieved from the files of our pathology department and reviewed in the aspects of morphological, immunophenotypic, presentation features, bone marrow infiltration and medical background. Chromogenic in situ hybridization by using the EBER probe and the immunohistochemical panel already stained on archival sections were reevaluated. The cases were subclassified into monomorphic and polymorphic subtypes, as well as germinal center B-cell (GCB) and non-GCB subtypes.
Results: The male to female ratio was 1.2 and the mean age at diagnosis was 65.7 years. At presentation, nodal involvement was observed in 62.06 % (18 of 29) and 10.3 % (3 of 29) of the cases were diagnosed on bone marrow biopsies. A total of 22.2 % (4 of 18) of cases exhibited bone marrow infiltration, thus stage IV disease.
Conclusion: In conclusion, it is very important to distinguish EBV positive DLBCL from other lymphomas or reactive processes and multi-institutional studies are required for the final definition of histologic, immunophenotypic, genetic, and clinical features of this entity.

PS-08-011

Paediatric marginal zone lymphoma of the parotid gland - a rare pathological entity

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Objective: Marginal zone lymphoma in the paediatric population is a very rare reported entity with an obvious male predominance (ratio 20:1) in children and prevalent involvement of cervical lymph nodes. In this report, we describe a particular case of this condition in a 12 years old female patient with marginal zone lymphoma of the parotid gland.
Method: The patient underwent parotid gland biopsy. Histopathological, mmunohistochemical and molecular assessments of the biopsy specimen were performed in order to establish the diagnosis.
Results: Histopathological examination revealed periductal lymphoid infiltrate associated with lymphoepithelial lesions and presence of germinal centers with marginal zone expansion. The monocytoid neoplastic lymphocytes were positive for CD20 and negative for CD3. Immunohistochemistry showed evidence of light chain restriction, with a kappa/lambda ratio of 5:1. Hemi-nested polymerase chain reaction, testing for immunoglobulin heavy-chain rearrangements, detected a clonal population at the level of FR2-JH region of the immunoglobulin heavy chains.
Conclusion: The histopathological, immunophenotypic and molecular findings are consistent with the diagnosis of paediatric marginal zone lymphoma of the parotid gland. Recognition of this entity can prove challenging as it might be difficult to distinguish between a paediatric marginal zone lymphoma and an atypical marginal zone hyperplasia with monotypic Ig expression.

PS-08-012

CD5 and CD30 expression in de novo diffuse large B cell lymphomas: A retrospective study

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Objective: Rare phenotypic aspects such as CD5-positive(CD5+), CD30-positive(CD5+) or"double expressor" diffuse large B-cell lymphomas(DLBCL) were found to have clinical and therapeutic implications. The aim of our study is to determine the aberrant expression of CD5 and CD30 in these lymphomas.
Method: We evaluate retrospectively 57 DLBCL (37 lymph nodes and 20 extranodal cases) diagnosed between 2013 and 2016. The specimens were obtained from 33 women(57.9 %) and 24 men(42.1 %), aged 23–82 years (mean age 59.54), untreated patients with no previous history of lymphoma.
Results: We found that 7(12.3 %) DBCL were CD5 + (>0 % cutoff), with a male predominance (1,3:1), 5 of them were classified as non-germinal center B-cell subtype(non-GCB) and all of them expressed bcl2 too; 19(33.3 %) were CD30+ using >0 % cutoff threshold and 9(15.8 %) with >20 % cutoff; the expression of bcl2 was higher in the group with 0–19 % CD30+ cells; 4(7 %) cases expressed both CD5 and CD30; most of CD5+ and/or CD30+ cases showed centroblastic monomorphic features.
Conclusion: Although the expression of CD5 and CD30 in DLBCL was noted in a minority of these patients, and their biology is incompletly understood, these markers should be performed in every case of DLBCL because they may influence the course of the disease.

PS-08-013

ERG1: Marker of lymph node sinus histiocytosis?

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Objective: We aimed to analyse the expression patterns of ERG1 in gallbladder neck lymph node sinus histiocytosis. The ERG1 antibody, detecting the protein coded by the V-ETS avian erythroblastosis virus E26 oncogene homolog, is used in the current practice for the immunohistochemical diagnosis of vascular and prostatic tumours.
Method: ERG1 protein was assessed by immunohistochemistry on gallbladder neck lymph nodes (identified on classical cholecystectomy specimens) with sinus histiocytosis.
Results: Nuclear ERG1 was expressed in intrasinus monocytes, in sinus histiocytosis lesions, of all studied lymph nodes (2 cases of drepancytosis and of lymph node lipopneumatosis each and, 1 case of C-hepatitis virus cirrhosis and of lymph node anthracosis each). As expected, lymph node endothelial cells (sinus or vascular) expressed ERG1. ERG1 expression lacked in extra-sinusoid macrophages of lymph node lipopneumatosis foci and of anthracosis.
Conclusion: The results of this study suggest a specific intrasinusoid expression of ERG1 in monocyte/histiocyte-type cells of lymph node sinus histiocytosis lesions besides the expression in endothelial cells.

PS-08-014

Epidemiological trends of follicular lymphoma in Poland

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Objective: In Western countries follicular lymphoma(FL) is one of the largest group of lymphocytic malignancies (20–40 % of all non-Hodgkin lymphomas). Contrary the low frequency of FL is observed in Eastern Europe. The aim of the study is to determine the incidence and epidemiological trends of FL in Poland.
Method: Data from the Polish National Cancer Registry for the years 2000–2014 are analyzed. The basic statistical indicators are applied: absolute numbers, percentages, crude rates(CR) and age-standardized rates(ASR).
Results: 3928 cases of FL with overall incidence CR0.68 and ASR0.46 are identified. The median age of onset is 61 and male to female ratio 0.86. The structure of morphological types of FL: NOS, grade 1, 2 or 3 are 72.58 , 4.81 , 12.88 , 9.73 % respectively. Among all collected mature B-cell lymphomas FL is placed next to BLL/CLL(CR 3.6), plasma cell neoplasm(CR 3.4), and diffuse B-cell lymphoma(CR 2.1).
Conclusion: Despite of increasing tendency of FL in Poland it comprises only 6.27 % of mature B-cell lymphomas. The etiology and pathogenesis of FL is not entirely understood but according to population-based case-control studies some environmental risk factors might have powerful impact on FL development. The differences of morphologic grouping between countries may result of variable diagnostic and registration criteria as well.

PS-08-015

One patient with two lymphomas: Report of three cases of simultaneous lymphomas

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Objective: Two simultaneous lymphomas in one patient are very rare. Most of the cases reported in the literature report simultaneous lymphomas in the gastrointestinal tract. We report the first two cases to our

knowledge of Simultaneous Primary Cutaneous Marginal Zone Lymphoma and Primary Nodal Follicular Lymphoma. One case of simultaneous Mantle cell lymphoma and LLC

Method: A 54 years old man with skin lesions in lower back and arms, adding to multiple hypermetabolic adenopathies with splenomegaly in PET-CT. A 58 years old woman with nodal follicular lymphoma presents an axillary nodular lesion. An 86 years old woman with chronic lymphocytic leukemia and breast cancer present cervical adenopathy. Skin biopsy, lymphadenopathy, Immunohistochemistry IHQ, flow cytometry, FISH, Monotypic light chain reaction and/or IgH gene rearrangement was performed in all cases.

Results: In first two cases, adenopathy showed a morphology of a low-grade follicular lymphoma. Skin lesions also showed a typical morphology of cutaneous marginal zone lymphoma. IHQ and flow cytometry study were compatible. Monotypic light chain reaction was detected in both cases. A simultaneous primary cutaneous marginal zone lymphoma with primary nodal follicular lymphoma was reported in both cases.In the third case, a Mantle cell lymphoma was reported after typical morphology and positivity of Cyclina D1 in IHQ and flow cytometry study were seen.

Conclusion: The presence of two lymphomas in one patient is very rare. A comprehensive diagnostic study is mandatory including microscopic, IHQ, flow cytometry, FISH, Monotypic light chain reaction and/or clonal IgH gene rearrangement, adding to clinical-pathological correlation.

PS-08-016

Label-free light microscopic imaging by auto-fluorescence identifies polymerised hemoglobin in erythrocytes of patients with sickle cell disease

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Objective: Fuorescence lifetime imaging (FLIM) measures the delay ("lifetime") of the emission of photons after stimulation of molecules by laser. FLIM images are constructed with their contrast created by transformation of lifetime values into pseudo-colors. Sickle cell anemia is characterized by hemoglobin polymerization in erythrocytes. Since the FLIM technique may indicate conformational changes, we tried to find out. whether lifetime changes could indicate areas of polymerized hermoglobin.

Method: We used unstained. air-dried blood smears of 10 patients with sickle cell anemia and of 25 patients without hematologic diseases. Images were captured with a confocal Zeiss Upright LSM780-NLO microscope and a HPM-100-40 Hybrid detector. Specimens were excited by a 405 nm pulsed diode laser at 80 MHz.

Results: Erythrocytes exhibited short lifetimes (210,4 ± 42,1 ps). Normally shaped erythrocytes in smears of sickle cell patients had similar values (207,7 ± 27,2 ps), whereas crenated erythrocytes (304,72 ± 43,9 ps). as well as drepanocytes (340.4 ± 66.3 ps), revealed significantly higher values. We could exactly localize the regions of higher lifetime values. which are equivalent to areas of hemoglobin polymerization.

Conclusion: The FLIM technique detected in polymerized areas increased lifetimes of hemoglobin autofluorescence, thus demonstrating precisely the topographic distribution of polymerized hemoglobin.

PS-08-018

Sclerosing angiomatoid nodular transformation of the spleen: Report of two cases and review of the literature

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Objective: Sclerosing angiomatoid nodular transformation (SANT) is a rare, benign, vascular lesion of the spleen. The lesion is usually asymptomatic and incidentally found on imaging. Its incidence, prevalence and pathogenesis are not well known. We report two cases of SANT diagnosed at our institution in 2 years.

Method: Both cases occurred in 45 years old patients. The first patient presented with a non-specific spongiotic dermatitis. A computed tomography (CT) scan performed to rule out an associated neoplastic condition showed an enlarged and heterogeneous spleen. The second patient underwent an abdominal CT scan as a routine investigation before renal transplantation which showed a 32 mm splenic nodule. Splenectomy was performed.

Results: In both patients, the macroscopic examination of the spleen revealed brownish pale stellate sub-capsular lesions of 3 cm and 4 cm respectively. Histological study confirmed the diagnosis of SANT showing a vaguely nodular splenic tissue with sclerosis and a proliferation of spindle cells admixed with inflammatory cells and siderophages surrounding areas of hypervascular red pulp.

Conclusion: Sclerosing angiomatoid nodular transformation of the spleen is a rare benign lesion that may simulate a malignant process on imaging. Till now, the final diagnosis can only be made on the basis of histopathological examination.

PS-08-019

Haematologic malignancy characterisation by anchored multiplex PCR and next-generation sequencing

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Objective: Hematologic malignancies can be driven by a diversity of mutation types, including single nucleotide variants, copy number variants, gene fusions, insertions and deletions and changes in gene expression profiles. However, comprehensive detection of driver mutations and signature gene expression profiles is challenging, as specific assays are required to detect each mutation type. We developed targeted NGS assays based on Anchored Multiplex PCR (AMP™) to simultaneously detect multiple mutation types and relative gene expression levels.

Method: AMP uses molecular barcoded (MBC) adapters and single gene-specific primers for amplification. Open-ended amplification permits identification of novel gene fusions, our bioinformatics algorithm enables FLT3-ITD detection and MBC adapters ligated to RNA fragments prior to amplification enable gene expression analysis.

Results: We demonstrate that AMP-based NGS identifies novel gene fusions relevant in blood cancers from a single end through breakpoint identification, with strand-specific amplification permitting bidirectional coverage for internal confirmation of fusion events. Furthermore, we optimized our bioinformatics algorithm to accurately detect ITDs along with concomitant point mutations in AML blood samples. Finally, MBCs enabled NGS-based expression profiling for identification of Diffuse Large B-Cell Lymphoma subtypes.

Conclusion: Our results demonstrate that AMP-based NGS enables comprehensive mutation and gene expression profiling of hematologic malignancies.

PS-08-020

Renal lymphoma: Clinicopathological evaluation of 25 cases

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Objective: Primary renal lymphoma is extremely rare and less than 100 cases are reported in the literature. Since lymphatic tissue is absent in kidney, it is considered that primary renal lymphoma originates from the lymphatics of the kidney capsule and then spread to the kidney parenchyma.

Method: Twenty-five cases diagnosed at our department as Non-Hodgkin lymphoma in the kidney biopsy or in nephrectomy material between 2000 and 2016 were reevaluated retrospectively.
Results: The diagnoses of the patients were as 12 diffuse large B-cell lymphoma (DLBCL), five extranodal marginal zone lymphoma, two Burkitt lymphoma (BL), two B-lymphoblastic lymphoma (LBL), two grade 2 follicular lymphoma (FL), one low grade B-cell lymphoma, one T-lymphoblastic lymphoma (T-LBL). Bone marrow biopsies were examined in 19 cases, only two cases presented neoplastic infiltration. Central nervous system involvement had been present in a case of T-LBL. Two cases of DLBCL manifested with coincidental nodal involvement and one had a previous diagnosis in the lymph node. In one case diagnosed as DLBCL, grade 3 FL was identified in the lungs and peribronchial lymph node. Nineteen cases were men and 6 cases were women. Mean age was 59.1 (range:11–80 years), all above 50 years of age except T-LBL and BL cases, plus a case of DLBCL.
Conclusion: Although observed rarely, a possibility of primary or disseminated hematological malignancy should also be considered when examining a case due to a mass in the kidney.

PS-08-021
Signet ring lymphoma: The import of immunohistochemistry in resolving diagnostic dilemmas
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Objective: To demonstrate the utility of ancillary methods in resolving diagnostic difficulties posed by atypical morphology in lymphoid neoplams.
Method: Antigen retrieval was performed on formalin fixed, paraffin embedded tissue blocks using the heat induced method. Indirect immunoperoxidase staining using a limited panel of monoclonal antibodies [Leucocyte Common Antigen(LCA), CD20 and CD3] was employed to determine the lineage of atypical/neoplastic cells with a signet ring morphology seen in a lymph node.
Results: Positive staining for LCA indicate that neoplastic cells are of hematopoietic origin. Positive staining for CD20 and negative staining for CD3 rules out a T cell lineage, while confirming a B cell origin.
Conclusion: Signet ring lymphoma should be entertained as a differential of lesions characterized by the presence of signet ring cells in lymph nodes. Immunohistochemistry is useful in determining the cell of origin in tumours with atypical morphology

PS-08-022
Regional panorama of paediatric Hodgkin lymphomas
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Objective: Hodgkin's lymphoma (HL) accounts for 40 % of childhood lymphomas. In the developed countries, which has a higher frequency of seeing after the second decade, and bimodal age distribution, is the first peak is in developing countries before adolescence. In developing countries, In this study, we aimed to evaluate of the prevalence of paediatric HL cases according to histopathologic subtypes, sex, age and the positivity rate of EBV infection.
Method: The total of 39 children with HL diagnosed between 2007 and 2017 in pathology department of İzmir Tepecik Training and Research Hospital were included in this study. Reports from the pathology laboratory archive of cases were reevaluated.
Results: The mean age was 2−18 ± 10 years in males, and it was 3 −18 ± 13.3 in females. Most tumours groups were located in cervical lymph nodes ($n = 37$, 95 %). Thirty-six cases (90 %) were alive, while 3 cases (9 %) were deceased. The presence rate of Ebstein Barr virus latent membrane proteins in RSCs was higher in mixed cellularity HL. EBV-LMP1 positivity was detected in 15 of 39 patients (38 %) immunohistochemically . The most of these patients ($N = 14$, 93 %) were mixed cellularity HL. Thirty-one cases (79.5 %) were mixed cellularity, 7 were nodular sclerosing and only one case (2.5 %) was lymphocyte depleted subtypes.
Conclusion: As a result of our study, the mixed cellularity subtype appeared more frequently. It was found that the incidence of 10–18 years of age in both male and female patients was higher than that of 0–9 year olds. EBV positivity was found to be high in the mixed cellularity HLs.

PS-08-023
A rare case of nasal lymphoma
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Objective: Extranodal NK-/T cell lymphoma, nasal type (WHO 2016) is an aggressive EBV associated disease representing only 1 % of all non-Hodgkin lymphomas in Europe and North America, with a male predominance. Higher prevalence exists in Asia and Central and South America.
Method: This patient presented with a right sided nasal mass, that infiltrated the right facial and nasal vestibular tissues.
Results: Microscopically surface epithelium was infiltrated by malignant lymphoid cells, plasma cells, immunoblasts, neutrophils and macrophages with ulceration. Marked angiocentricity, angioinvasion and thrombosis were present. Necrosis of the lymphoid cells and prominent karyorhectic debris was present. The destructive process involved cartilage and bone spicules. Immunohistochemistry was strongly positive for CD2, CD3, CD4, CD8, CD30, CD56, CD43, Granzyme B and EBV and negative for CD20, CD5, CD79a. Ki67 index 90 %.
Conclusion: As extranodal NK/T cell lymphoma, nasal type, may clinically mimic other destructive disease entities affecting mid-facial structures including other lymphomas, nasopharyngeal squamous cell carcinoma, tertiary syphilis, granulomatosis with polyangiitis and fungal infections, the definitive diagnosis must be based on histopathological and immunological studies.

PS-08-024
An unusual presentation of extranodal Rosai-Dorfman disease
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Objective: We report a case highlighting an extranodalRosaiDorfman Disease (RDD) with concomitant cutaneous and breast tissue involvement of RDD without any lymphadenopathy, which has rarely been reported in the literature.
Method: We reported a case of a 57-year-old woman, previously healthy, who was seen with erythematous indurated papules of the face, mimicking xanthoma or sarcoidosis. On examination there was a breast nodule without any lesions elsewhere in the body.Biopsies of the affected tissue were subjected to histopathological examination.
Results: The histopathological examination showed a mixed cellular infiltration, predominantly composed of histiocytes that was mixed with lymphocytes including plasma cells andpolymorphous nuclear leucocytes.The histiocyteswere filledwith pink cytoplasm and contained inflammatory cells demonstrating emperipolesis. The diagnosis of RDD was established.
Conclusion: Rosai–Dorfman disease (RDD) is a rare proliferative histiocytic disorder,characterized by persistent massive lymphadenopathy mimicking malignant tumours. Extranodal RDD is uncommon, cutaneous lesions can occur in about 10 % of patients,the breast involvement is exceptional. Moreover extranodalRDD without any lymph node involvement is particularly rare. The disease may be under recognized and considered to be a diagnostic challenge.

PS-08-025

Clinico-hematological spectrum of myeloproliferative neoplasms: Study from a tertiary care hospital in India

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Objective: Myeloproliferative neoplasms (MPN) include BCR-ABL positive chronic myelogenous leukemia (CML), polycythemia vera (PV), primary myelofibrosis (PMF) and essential thrombocythemia (ET). The incidence, prevalence and clinic-hematological profile of patients during a 3 year study period are presented.
Method: Cases of MPN diagnosed according to WHO (2008) criteria from January 2012 to December 2014 were included in the study. BCR-ABL fusion gene was tested in all cases. Diagnosis of PV, ET and IMF were based on clinical, hematological and marrow biopsy, JAK2V617F mutation was tested in few cases.
Results: Of total 464 cases of MPN, CML was the most common (380 cases, 81.7 %) and 84 patients had BCR-ABL negative MPN including 19 cases each of ET and IMF, 12 cases of PV and 34 diagnosed as unclassifiable MPN. All cases of PV were diagnosed in overt phase. Mean age for CML patients was 38.5 years. Most CML patients were in the intermediate risk category (Sokal and Hasford scoring). IPSET score was low in most of the ET patients (47.3 %). IPSS score in most cases of IMF showed intermediate-1 risk group. JAK2V617F mutation was positive in 12/ 33 cases.
Conclusion: We observed differences in prevalence, age, gender in all types of MPN compared to western data. The prevalence of BCR-ABL positive CML was much higher, Polycythemia Vera was the least common. MPN occurred at a younger age and hematological severity was more pronounced.

PS-08-026

Polymorphic posttransplant lymphoproliferative disorder in a heart transplanted patient

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Objective: Introduction Posttransplant lymphoproliferative disorder (PTLD) is a frequently fatal complication of immunosuppression with varying incidence, approximately in 1–2 % heart transplanted patients, usually (80–90 %) associated with Epstein-Barr virus infection. Patients with PTLDs have a high mortality rate (50–80 %). Polymorphic type of PTLDs present as a destructive B-cell lesions revealing a full range of B-cell maturation.
Method: Case presentation A 46-year-old male patient underwent a heart transplantation due to severe ischaemic cardiomyopathy. The early postoperative period was unremarkable, but 3 months after the transplantation signs of allograft rejection (ISHLT rejection grade 1B-1R) appeared. Despite the administered therapy, the patient's condition worsened with fever and he suffered cardiorespiratory arrest. Electromechanical dissociation was declared the cause of death. Autopsy revealed an extremely hypertrophic and dilated heart (900 g) and a poorly delineated pale yellow mass occupied the right atrium, surrounding the pulmonary artery sutures.
Results: Histopathology Histologically, tumour was partially necrotic, consisted of B- and T-lymphocytes, plasma-cells, immunoblasts, Reed-Stenberg-like cells and lymphoplasmacitoid cells, as confirmed by immunohistochemistry. Tumour growth was destructive, infiltrating pericardial fat tissuse and atrial muscle.
Conclusion: Conclusion EBV-assocciated polymorphic PTLD presents a serious complication in heart transplanted patients. Causing myocardial injury, polymorphic PTLD could cause fatal heart failure.

PS-08-027

A rare entity of primary cutaneous, extranodal NK/T-cell lymphoma, nasal type with loss of CD56 expression; Case report

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Objective: Extranodal NK/T-cell lymphoma (ENKTCL), nasal type is an aggressive Epstein Barr virus (EBV) associated NK/T cell neoplasm with poor prognosis. Ekstranasal type NK/T cell lymphoma is less common than nasal type. We report a unique case of a CD56-negative, Epstein-Barr virus (EBV)-positive ENKTCL, nasal type, with cutaneous involvement.
Method: A 52 year old female presented to the hospital of a 6 × 4 cm measured, indurated, ulcerative soft tissue mass on her forearm. Dermal biopsy was performed. Histopathologic examination showed a nodular patterned, atypical lymphocytic infiltration, composed of medium-large sized cells with irregular nuclei, inconspicuous nucleoli and high proliferative activity. The neoplastic cells stained positively for antibodies against surface CD3, CD2, Granzyme and Perforin, whereas they were negative against CD4, CD8, CD56, CD20 and CD30. EBV-encoded RNA (EBER) in situ hybridization was widespread positive on the neoplastic cells.
Results: Nodal or ekstranodal involvement except for the initial localization of the tumour was not detected on the PET-CT images. EBV positive primary cutaneous ENKTCL was diagnosed on the patient.
Conclusion: Primary cutaneous ENKTCL is a rare entity with poorly defined clinicopathologic features. Although CD56 expression is prototypic, loss of CD56 expression may be demonstrated on some of ENKTCL's and this possibility should be kept in mind on virally associated cutaneous T cell lymphomas.

PS-08-028

Neural cell adhesion molecule (CD56)-positive B-cell lymphoma of the urinary bladder

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Objective: Herein, we describe the first documented case of primary CD56-positive B-cell lymphoma (diffuse large B-cell lymphoma, DLBCL) of the urinary system.
Method: A 60-year-old Japanese woman presented with recurrent cystitis. MRI revealed a sessile tumour protruding into the bladder lumen, with destruction of the muscularis propria. Systemic CT detected no other suspicious lesions.
Results: The transurethral biopsy specimen showed diffuse proliferation of medium to large neoplastic cells with high nuclear/cytoplasmic ratios and numerous mitotic figures (98/10HPFs). Immunohistochemically, neoplastic cells were positive for LCA, CD20, CD79a and CD56, while being negative for CD3, CD5, CD38, CD138, cyclin D1, chromogranin A, synaptophysin and cytokeratin AE1/AE3. Furthermore, this DLBCL had a non-germinal center B cell-like phenotype (i.e. CD10 negative, with Bcl-6/MUM1 positivity). Epstein-Barr virus-encoded RNA in situ hybridization (EBER-ISH) yielded negative results.
Conclusion: It still remains to be determined why CD56 expression can be present in some B-cell lymphomas as well as whether or not it plays a key role in the prognosis of DLBCL. Our patient with an extranodal CD56+/Bcl-6+/CD5- DLBCL, interestingly, showed a good response to rituximab and THP-COP and has remained in complete remission for 12 months. (J Clin Pathol. 2016; 69: 89–92).

PS-08-029

The cell cycle regulation roles of p15INK4b, p16INK4a and p21WAF1/CIP1 in multiple myeloma cells treated with HDAC inhibitors

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Objective: The disruption of normal mitosis by histone deacetylase (HDAC) inhibitors is a significant contributor to the anticancer effects of these drugs. HDAC inhibitors are known to arrest human tumour cells at the G1 phase of the cell cycle and activate cyclin-dependent kinase (CDK) inhibitors. One of the regulators of cell cycle progression is the cyclin-dependent kinase inhibitor p21WAF1/CIP1, CDKN1A gene of the CIP/KIP family. The p15INK4b and p16INK4a encoded by CDKN2B and CDKN2A genes, belong to the INK4 family proteins. The aim of our study was to determine the sensitivity of human multiple myeloma cells to HDAC and CDK inhibitors as well.
Method: To determine HDAC and CDK inhibitors influence on cell cycle regulation, DNA content was assessed by flow cytometry analysis. Gene expressions of CDKN1A, CDKN2A and CDKN2B were followed in CCL-155 (RPMI-8226) human multiple myeloma cells cultured with HDAC inhibitors SAHA (suberoylanilide hydroxamic acid) and SBHA (suberic bishydroxamata) and CDK inhibitor JNJ-7706621 with the highest affinity to CDK1/2.
Results: In the present study p21WAF1/CIP1 was expressed at a similar level in all types of cell treatments. The CDK p15INK4b expression in cells treated with SAHA and JNJ inhibitors was considerably increased while in SBHA treated cells we detected unchanged expression.
Conclusion: The expression of analysed cyclin dependent kinases from both the CIP/KIP and INK4 family CDK proteins probably does not dependent on the type of used HDAC inhibitors. This study was supported by grants LF_2017_021 and NPS I LO1304 from the Czech Ministry of Education.

PS-08-030

Differences in morphometric parameters of megakaryocytes in patients with essential thrombocythemia with detected JAK2 or CALR mutation

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Objective: JAK2- and CALR-mutated essential thrombocythemia (ET) cases are of the greatest scientific interest, because these mutually exclusive mutations are observed in more than 80 % of patients. We attempted to evaluate changes in megakaryocyte size and composition in JAK2- and CALR-positive ET cases by using a morphometric method.
Method: We examined 48 bone marrow samples from patients with ET. The patients were divided, depending on whether they had a JAK2 mutation ($N = 26$) or a CALR mutation ($N = 22$). In each sample 100 megakaryocytes were randomly selected and analyzed to determine cell area (Sc), nucleus area (Sn) and nuclear shape factor ($Fn = Pn/(2*Sn/\sqrt{(Sn/\pi)})$, where Pn is the perimeter of the nucleus. To determine if the differences between the two groups were statistically significant, we used repeated measures ANOVA. The differences were considered to be significant when $p < 0.05$.
Results: Morphometric characteristics of megakaryocytes in patients with JAK2-mutated ET: Sc = 617.9 ± 287.2 μm2, Sn = 159.9 ± 88.7 μm2, Fn = 1.42 ± 0.28. Morphometric characteristics of megakaryocytes in patients with CALR-mutated ET: Sc = 669.7 ± 307.2 μm2, Sn = 180.4 ± 88.0 μm2, Fn = 1.52 ± 0.32. Differences were found to be statistically significant ($p < 0.05$).
Conclusion: The observed morphometric differences in megakaryocytes allow us to propose a pathogenic effect of mutation status on the phenotype of the tumour clone.

PS-08-031

Aberrant immunophenotypic characteristics of six clinicopathologically diverse cases of plasmablastic lymphoma

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Objective: Plasmablastic lymphoma (PBL) is considered a rare subtype of large B-cell non-Hodgkin lymphoma, occurring predominantly in the oral cavity of human immunodeficiency virus (HIV) + patients. The clinicopathologic characteristics of two cases of HIV+ and four cases of HIV- PBL are herein presented.
Method: All cases were retrieved from the archives of our pathology department. An extensive immunohistochemical study on 3 μm-thick sections of formalin fixed paraffin embedded tumour tissue was performed in all cases, based on material adequacy.
Results: All HIV- cases were found at extra-oral locations (half of them in the gastrointestinal tract) of much older individuals (mean age: 75) than the two oral cavity cases of HIV+ patients (mean age: 43). One HIV- case was CD30+, while CD31 positivity was also observed in some of the cases, regardless of HIV status. Aberrant T-cell marker positivity in various combinations was found in one HIV+ case (CD3/CD4) and three HIV- cases (CD43 and CD7/CD43).
Conclusion: Clinicians and pathologists should generally be aware of extra-oral, HIV- PBL, which may morphologically and immunohistochemically masquerade as a T-cell lymphoma, a CD30+, anaplastic, large cell lymphoma or a poorly differentiated, epithelioid, vascular neoplasm.

PS-08-032

TTF-1 expression in diffuse large B-cell lymphoma: An unusual but tricky phenomenon

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Objective: Thyroid-specific transcription factor 1 (TTF-1) is a transcription factor encoded by the NKX2-1 gene. TTF-1 expression is assumed to be restricted to pulmonary and thyroid epithelium. We recently encountered a diffuse large B-cell lymphoma (DLBCL) in a man with a history of pulmonary adenocarcinoma, which showed nuclear expression of TTF-1/SPT24. This study aimed to evaluate TTF-1 expression in a large cohort of DLBCL, using two commercially available monoclonal antibodies (clones 8G7G3/1 and SPT24).
Method: Tissue blocks originated from 32 DLBCL patients diagnosed at the University Clinics St Luc (Brussels, Belgium), and 72 DLBCL patients from Ghent University Hospital (Ghent, Belgium). Immunohistochemistry was performed on whole mount slides in an ISO15189 accredited lab at Ghent University Hospital. Both nuclear and cytoplasmic TTF-1 expression were evaluated.
Results: None of the DLCBL presented cytoplasmic TTF-1 expression. Nuclear TTF-1 expression was detected in four DLBCL (4 %) by the SPT24 clone. Nuclear TTF-1 staining was not observed when the 8G7G3/1 clone was applied.
Conclusion: The 8G7G3/1 and SPT24 clones are widely used, but our study shows that the SPT24 clone might result in false positive TTF-1 expression in DLBCL. This could present an important diagnostic pitfall in the investigation of poorly differentiated malignancies.

PS-08-033

BCL2, BCL6 and CMYC abnormalities in 44 Turkish patients with diffuse large B-cell lymphomas

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Objective: Diffuse large B-cell lymphoma (DLBCL) presents remarkable heterogeneity at the clinical, histopathological and molecular levels. Commonly observed genetic abnormalities that likely contribute to pathogenesis include translocations of BCL6, BCL2, and cMYC. In this study, we investigated 44 cases of DLBCL for cytogenetic abnormalities of BCL2, BCL6, and cMYC genes by FISH, as well as for immunohistochemical expressions of BCL2 and BCL6.
Method: A total of 44 patients with DLBCL were retrospectively analysed. We reevaluated all slides stained with hematoxylin eosin and reports from the pathology laboratory archive of cases. We also performed immunohistochemistry and FISH analyses of these cases.
Results: The mean age was 61.5 (range 20–86) years. Most tumours ($n = 26$) were located in the extranodal cites. Presence rate of cytogenetically abnormalities in BCL6, BCL2, and cMYC genes were 11(25 %), 2 (4.5 %) and 4 (9.1 %), respectively. Immunohistochemical expressions of BCL2 (n = 20, 45.5 %) and BCL6 (n−12, 27.5 %) were more common. Interestingly both immunhistochemical study and FISH analysis demonstrated that presence rates of expression and/or abnormalities BCL2 and BCL6 were higher in tumours located in extra nodal cites and/ or visceral organs.
Conclusion: Nowadays several genetic abnormalities have been identified in subsets of DLBCLs. The 3 most frequently deregulated genes; BCL6, BCL2, and cMYC which affect the regulation of B cell development. In this study, we found that the break apart of BCL6 gene was the most common genetic abnormalities in DLBCL similar to the results of previous studies. However, the rates of these molecular abnormalities were lower than other studies. This situation was thought to be related with geographic difference.

PS-08-034

FLT3-ITD and NPM1 mutations in acute myeloid leukemia patients with cytogenetically favourable - or intermediate - risk

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Objective: While FLT3-ITDmutations in patients with intermediate cytogenetic risk are also associated with a poor prognosis, patients with intermediate cytogenetic risk but who harbor Nucloephosmin(NPM1)mutations without the FLT3-ITDmutation have a better risk status.
Method: A total of 38 AML patients were investigated with quantitative PCR method.
Results: Fourteen patients with cytogenetically favorable risk were 14(37 %) and intermediate risk was 24 (63 %). None of the patients with favorable cytogenetic risk did have NPM1 mutations, but three of these patients(21 %) had FLT3-ITD mutations with t(15;17) translocation. In intermediate cytogenetic risk group, 11 patients (54 %) had FLT3-ITD mutations and 13 patients(46 %) had NPM1 mutations. While the median age of all AML patients was 52 years, it was 59 years in the intermediate cytogenetic risk group with FLT3-ITD mutations.
Conclusion: FLT3-ITDmutations are not rare events in either favorable or intermediate cytogenetic risk AML groups. Since the presence of FLT3-ITDmutations is associated with adverse prognoses, all patients who are suspected of having AML should be screened for the mutation status of FLT3 gene, even those in the cytogenetic risk group with a favorable prognosis. The median age of the patients with an FLT3-ITDmutation was greater than that of the patients without the mutation. While the reason for the discrepancy observed between the median ages of the two groups is unclear, it is certain that in order to better understand any relationship between age and the FLT3-ITDmutation, further investigations are necessary.

PS-08-035

ALK + large B-cell lymphoma: Report of 3 cases

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Objective: Diagnosis of ALK + large B-cell lymphoma (ALK + LBCL) is challenging due to its rarity, morphologic and immunophenotypic similarities to other hematologic and non-hematologic neoplasms. The aim of this study was to review the clinicopathological characteristics of all ALK + LBCL diagnosed in our institution and to find eventual misdiagnosed cases among lymphomas that enter its differential diagnosis.
Method: In our database we've found 3 cases of ALK + LBCL diagnosed only in the last 3 years. To exclude eventual pitfalls since its definition in 2008, we've searched our database for all cases of CD20-diffuse large B cell lymphomas (CD20-DLBCL), ALK + anaplastic large T-cell lymphomas, plasmablastic lymphomas (PBL), plasmablastic plasmacytomas (PBP), primary effusion lymphomas (PEL), HHV8 + LBCL in the period 1.1.2008–1.1.2017. Additional immunohistochemical stainigs were performed in doubtful cases.
Results: 8 cases of CD20-DLBCL, 41 cases of ALK + ALCL, 9 cases of PBL, 7 cases of PBP have been revised. We've found no cases of PEL and HHV + LBCL and no cases of misdiagnosed ALK + LCBL. Clinicopathological features of diagnosed ALK + LBCLs are shown (Table 1).
Conclusion: Diagnosis of ALK + LBCL is demanding. To exclude eventual pitfalls, wide pannel of immunohistochemical stainings is necessity. We'have found no cases of misdiagnosed ALK + LBLC among lymphomas that enter it's differential diagnosis although non-hematological neoplasms that could mimick it haven't been revised.

PS-08-036

The correlation between plasma cell morphology and chromosomal abnormalities in myeloma cells detected with fluorescent in situ hybridisation (FISH)

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Objective: To investigate the possible connection between morphological features of plasma cells(PC) and some of the most frequent chromosomal abnormalities in multiple myeloma (MM).
Method: Bone marrow aspirate smears taken at the moment of diagnosis were analyzed for: del(13q14), del(13q34), del(17p), t(4;14) and t(14;16). Smears were stained according to short May-Gruenwald-Giemsa(MGG) protocol, areas with abundance of myeloma cells marked, slides destained, and the FISH analysis performed on selected areas. On MGG-stained slides, the frequency of morphological features and morphometrical data were assessed - chromatin, nucleoli, irregular nuclei, multinuclearity, paranuclear halo, "flaming" PCs, ragged cytoplasm, cytoplasmatic budding, Russell bodies, longest nuclear (ND) and cytoplasmatic diameter (CD) and the ND/CD ratio. The correlations were analyzed using t-test.
Results: FISH was successful on 120/169 smears. The incidence of chromosomal abnormalities was as expected from the literature, only del(17p) showed higher frequency. Del(13q14) was correlated with a higher proportion of PCs with ragged cytoplasm. Del(13q14) and del(13q34) were connected with more multinucleated PCs. Cases with del(13q14) had lower ND/CD ratio. Patients with t(4;14) had more frequent Russell bodies.
Conclusion: Some morphological features of PCs in MM, seen in BM aspirates, could provide a hint towards the presence of certain chromosomal abnormalities with prognostic significance.

PS-08-037

Osteopontin expressing macrophages predict survival in diffuse large B cell lymphoma

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Objective: Osteopontin (OPN) is cell adhesion molecule and cytokine expressed by many tumour cells as well as tumour associated macrophages (TAMs). The aim of this pilot study was to analyse the prognostic significance of osteopontin expressed by TAMs in patients with diffuse large B-cell lymphoma (DLBCL).
Method: The expression of osteopontin in TAMs was analyzed immunohistochemically on tissue microarrays of 81 DLBCLs. OPN expression was scored semiquantitatively as low, moderate or strong. The level of OPN expression in TAMs was correlated with clinicopathological data and overall patient's survival.
Results: Low OPN expression was found in 32 cases (40 %), moderate in 31 (38 %) and strong in 18 cases (22 %). High level of OPN expression in TAMs was associated with increased international prognostic index ($p < 0.001$) and high serum LDH level. There was a trend toward the association of low OPN level and complete response to therapy ($p < 0.06$). Also, higher level of OPN expression in TAMs was associated with poor overall survival ($p < 0.04$).
Conclusion: OPN expressed by TAMs is potential prognostic factor in DLBCL patients.

PS-08-038

Synchronous presentation of two extranodal lymphomas: Follicular lymphoma and extranodal marginal zone lymphoma of the mucosa associated lymphoid tissue (MALToma)

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Objective: Herein, we report a case of syncronous MALT and follicular lymphoma in a patient's two different extranodal tissues.
Method: A male patient of 78 years old, applied for dyspepsia. All the laboratory tests were in normal ranges,The endoscopic biopsy revealed a slightly diffuse, submucosal lymphoid infiltration of small lymphocyts with no evident lymphoepithelial lesions. The neoplastic cells immunostained positively with only CD20, CD43 and bcl-2 with a Ki67 proliferation rate of 3–5 %. The diagnosis was given as MALT lymphoma with no bone marrow infiltration. Increased 18-FDG involvement was found in milimetric nodular opacities seen in the left apex, left upper lingular segment of the left lung and middle lobe medial segment of the right lung. In microscopic evaluation of the lung, a small lymphocytic infiltration predominantly with nodular and follicular patern was observed. The neoplastic cells showed diffuse immunexpression of bcl-2, bcl-6, CD20 and CD10. The diagnosis of the lung biopsy was given as follicular lymphoma grade 3A with a rate of Ki67 25 %.
Results: The diagnosis was given as MALT lymphoma with no bone marrow infiltration. The diagnosis of the lung biopsy was given as follicular lymphoma grade 3A with a rate of Ki67 25 %.
Conclusion: Multiple lymphomas may rarely occur simultaneously and cause diagnostic problems in hematology practice. The firstly diagnosed malignancies may shade the synchronous disease. As in our case, symptoms may overlap causing delay of the synchronous neoplasm. But an atypical presentation should remind a synchronous neoplasm and the treatment needs to be planned including both diseases.

PS-08-039

Extramedullary hematopoiesis in adults: Review of cases in Cruces Universitary Hospital over the last 20 years

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Objective: The aim of this study is to classify the cases of extramedullary hematopoiesis in adults, specially in spleen and liver, and to emphasize its relationship with myeloproliferative and myelodisplastic disorders
Method: Retrospective study of the medical records and archival tissue sections of all cases with a diagnosis of extramedullary hematopoiesis in Cruces University Hospital between 1997 and 2017
Results: We found 10 cases, with a mean age of 61.6 years (range 50–76). A slight male predominance was noted (6 cases, 60 %). Clinically, all pacients showed hepato and splenomegaly. Curiously, in 1 case the involvement manifested as an intrahepatic nodular mass-like lesion. In 6 cases (60 %), extramedullary hematopoiesis was associated with hematological diseases (myelofibrosis, thalassemia, polycythemia vera), while two other cases were found in a context of malignancy (lymphoma, advanced pulmonary adenocarcinoma)
Conclusion: Extramedullary hematopoiesis is a compensatory mechanism by which blood cells are produced outside the bone marrow, when marrow production is unable to maintain the needs of the organism. It can be seen in a variety of hematological disorders that lack cell formation such as myelofibrosis. Most of the times the involvement is microscopic, but it may sometimes ocurre as organomegaly or mass, like one of the cases we have presented here

PS-08-040

A case of "hairless" hairy cell leukemia

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Objective: Hairy cell leukemia (HCL) is a low-grade, chronic B-cell leukemia that comprises approximately 2 % of leukemia cases and often occurs in middle-aged men. We report a case of HCL that was diagnosed by assessment of distinctive pathological and immunohistochemical features.
Method: A 69-year-old man was referred to our hospital because of a white blood cell count of 1,800, found on routine physical examination.
Results: Bone marrow biopsy showed hypercellular features with infiltration by monotonous cells. The cells had a central single small nucleus and abundant cytoplasm, a so-called "fried egg appearance", which suggested the diagnosis of HCL. The peripheral blood smear showed malignant cells with no cytoplasmic projection. Flow cytometry examination revealed the tumour cell positivity for CD20, CD103 and CD123, which are characteristic of HCL. As the patient was diagnosed with symptomatic HCL, he was started on cladribine, a purine analog. Bone marrow biopsy showed a decreased number of small lymphocytes after that treatment.
Conclusion: This HCL case had all the typical immunophenotypic characteristics of HCL, except for CyclinD1 and having no cytoplasmic projections, which would have suggested splenic marginal zone lymphoma, HCL-variant, or other diseases. We encountered a case in which the pathological features and immunophenotype enabled a definite diagnosis of "hairless" HCL.

PS-08-041

A case of recurrent primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoproliferative disorder

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Objective: Primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma remains a provisional entity according to the recent update of WHO classification. An unusual case of this entity characterized by two different cutaneous lesions in a time interval of 9 years is discussed.
Method: A 62-year-old man presented with a cutaneous tumour of the sculp. The patient had a history of a cutaneous lesion of the back, which appeared 9 years ago. That lesion had been totally excised and no other treatment was received.
Results: Hematoxylin and eosin stained sections from both lesions showed a partly nodular infiltration, involving the dermis and the subcutis, characterized by small to medium-sized pleomorphic T- lymphocytes with round or irregular nuclei and often distinct nucleoli. Varying numbers of intermixed histiocytes, plasma cells, eosinophils, B- cells and reactive cytotoxic cells were present. Scattered large cells were also identified. Immunohistochemically, the cells expressed CD45RO, CD2, CD3, CD5 and CD4 whereas CD7 and CD43 antigens showed reduced expression. PCR analysis was performed on both biopsies and revealed TCRβ and TCRγ rearrangements.
Conclusion: As demonstrated by this case total excision in localized disease show long term effectiveness, but it can recur in another anatomical site even after many years.

PS-08-042

Expression of CD34-positive progenitors in fetal human liver hematopoiesis

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Objective: In humans, the liver represents the major hematopoietic organ during gestation, as it provides circulating blood cells to the developing fetus. Given this fundamental function, we investigated the presence of liver hematopoietic stem cells at different weeks of gestation.
Method: Liver tissue specimens, obtained from ten fetuses with a gestational age ranging from 10 to 36 weeks, were stained with H&E and immunostained with an anti-CD34 monoclonal antibody. The hematopoietic activity was evaluated according to previous works (1) and the presence of CD34+ cells.
Results: Hematopoietic activity ranged from stage II and III in earlier weeks of gestation, to stage IV in the latest weeks before birth. In all liver specimens, isolated and scattered CD34+ cells in the hepatic parenchyma in close contact with developing hepatoblasts were identified.
Conclusion: The presence of CD34+ progenitors cells in the human fetal liver during gestation, most likely represent hematopoietic stem cells. The finding of CD34+ cells confirms previous data suggesting that hematopoietic stem/progenitor cells could migrate to the liver during the early phases of embryonic development (1). Further studies on a large series of fetal liver might clarify the role of CD34+ stem/progenitors in liver hematopoiesis during fetal life and could provide new insights on the role of hematopoietic precursor cells in pathological conditions. REFERENCES 1. Fanni D, Angotzi F, Lai F, Gerosa C, Senes G, Fanos V, Faa G (2017) Four stages of hepatic hematopoiesis in human embryos and fetuses. The Journal of Maternal-Fetal & Neonatal Medicine 1–7.

PS-08-043

Four cases with cytopenia due to Temozolomide's bone marrow toxicity

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Objective: Temozolomide(TMZ) is an alkylating agent, used mainly for the treatment of high-grade gliomas. Although it is well-tolerated, rarely hematopoetic adverse effects, that are usually reversible, are reported.
Method: We present 4 cases with high-grade glial tumours (2 glioblastoma, 2 anaplastic astrocytoma) who develop cytopenia after TMZ usage.
Results: Three of the patients are females. Average age was 55 (range; 35–73) years old. All of the patients developed cytopenia in 1–3 months interval after TMZ. All had bone marrow(BM) biopsies. Two of them had BM selularity ranging 1–5 %, consistent with aplastic anemia(AA). They died due to hematopoetic toxicity. Other two patients had normocellular BM with dysplasia in hematopoetic cells without increased blast number. None of them had reticuline fibrosis. They accepted as secondary MDS. Cytogenetic investigation showed no chromosomal abnormality. These patients recovered cytopenia after neupogen and thrombocyte apheresis.
Conclusion: The most reported hematopoetic side effects of TMZ are mild-severe cytopenia, AA, secondary MDS, acute myeloid/lymphoblastic leukemia. Patients are frequently females. AA seems unique to TMZ and MDS/leukemia latency is shorter when compared with other alkylating agents. Dead can occur after BM suppression. Physicians should be aware of TMZ's cytotoxic and mutagenic properties on BM.

PS-08-045

Mediastinal granulomatous lymphadenitis accompanying tumours

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Objective: Granulomatous inflammation may be accompanied with tumours. It may be present in the lymph node, which the tumour cells drain or distant lymph nodes without metastasis. The exact pathogenesis of granulomatous reactions accompanying tumours is not clear. It is thought that tumour immunity plays a role in cases with unidentified etiology. In present study, we aimed to detect the relationship between mediastinal granulomatous lymph nodes of patients with tumour diagnosis, which were suspicious for metastasis by radiology.
Method: Totally 39 patients with mediastinal granulomatous lymphadenitis also having tumour diagnosis were included in the study. Mycobacterium tuberculosis was searched in all cases by Polymerase chain reaction (PCR).
Results: Fifteen cases were male, 24 were female. Mean age was 57 (22–74 years). Diagnoses of the tumours were as follows, subsequently; 10 lung cancer, 9 breast cancer, 7 gastrointestinal tract, four endometrium cancer, three skin melanoma, two lymphoid neoplasm, two malignant mesenchymal tumour, one larynx carcinoma, one thymoma. Twelve cases included necrosis in granulomas, 27 cases were without necrosis. M. tuberculosis was detected by PCR in five cases.
Conclusion: Hence, granulomatous lymphadenitis may mimic malignancy both with radiology and positron emission tomography (PET). Histopathologic evaluation should be performed to suspicious lymph nodes to prevent overstaging.

PS-08-046

Richter's transformation of a B cell non Hodgkin lymphoma of the subtype chronic lymphatic leukemia with aberrant MYC/IGH t(8;14) translocation and 17p(TP53) deletion: A case report

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Objective: The chromosome translocation t(8;14)(q24;q32) activating the MYC oncogene was first described in Burkitt lymphomas. It also seems to play a role in the Richter's transformation of a low grade B cell lymphoma to a high grade lymphoma. We present a case of a patient with the transformation of a low grade B cell non Hodgkin lymphoma of chronic lymphatic leukemia (B-CLL) subtype to a diffuse large B cell lymphoma (DLBCL). An aberrant MYC/IGH t(8;14) translocation and a 17p(TP53) deletion were detected via fluorescence in situ hybridization (FISH).
Method: Two biopsies of a 79 year old patient showed manifestations of a B-CLL. Due to isolated blast-like lymphocytes and an increased Ki-67 labeling index a FISH-analysis to detect MYC/IGH t(8;14) translocations and 17p(TP53) deletions was performed.
Results: FISH-analysis revealed a MYC/IGH t(8;14) translocation with an aberrant expression pattern indicating a polysomy of the derivative chromosome 14 or 8 and also a 17p(TP53) deletion.
Conclusion: Roughly 8 % of B-CLL patients will develop a DLBCL. A TP53 dysfunction in combination with a MYC activation have been described as relevant molecular changes in the course of this so-called Richter's syndrome. This case showed typical cytomorphology, increased Ki-67 labeling index, a MYC/IGH t(8;14) translocation, a 17p(TP53) deletion as well as an agressive course of disease which confirms the diagnosis of Richter's syndrom.

PS-08-047

Gaucher disease diagnosed in an adult: Rare cause of hepatosplenomegaly in adult age group

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Objective: Gaucher disease is the most common autosomal recessive lysosomal storage disease worldwide generally diagnosed in childhood. The most common presentation of the disease is hepatosplenomegaly. It is generally seen in paediatric age group.
Method: Nineteen year old woman applied with weakness with no medical history. The laboratory results were normal and ultrasonography revealed hepatosplenomegaly confirmed coloured Doppler with no vascular abnormalities. After that a bone marrow biopsy was performed.
Results: In bone marrow aspirates, macrophages with abundant sea-blue, "crumpled tissue paper" cytoplasms were observed. By immunohistochemical examination these cells with large cytoplasms were positive with CD68, lyzozyme and TRAP but negative for S100 and CD1a. The histomorphologic features were reported as concordant with Gaucher disease. The diagnosis was confirmed by enzymatic activity and genetic studies.
Conclusion: In cases with unexplained hepatosplenomegaly, Gaucher disease should be kept in mind even in adult age group. The gold standart for the diagnosis is to measure the enzymatic activity of glucocerebrosidase. Enzymatic replacement is the main treatment modality for these cases.

PS-08-048

Primary MALT lymphoma of urinary bladder (PMLUB): On occasion of two cases

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Objective: Lymphoma of urinary bladder is rare, comprising 5 % of non-urethelial tumours. Less of 100 cases have been reported. It can be either primary or secondary, the former extremely rare comprising 0.2 % of extranodal lymphomas. The most prevalent subtype is Malt- lymphoma, affecting adults older than 60 years. We describe two cases of PMLUB.
Method: The patients, a 81-year old woman and a 63-year old man, complaining for hematuria and dysuria, presented wide based submucosal masses at cysteoscopy. The preoperative diagnosis was urothelial carcinoma. Transurethral biopsies were performed. A combined chemotherapy (R-CHOP) was administered. After a 34 and 8 months, respectively, follow up period, both patients are without signs of recurrence or metastasis.
Results: On histology, both subepithelial tumours consisted of small size monotonous lymphoid cells with centrocytoid or monocytoid appearance with focal plasmatocytoid features. There was urothelium ulceration and focal infiltration of muscularis propria. Tumour cells were immunoreactive for LCA, CD20, BSAP, BCL2 with low Mib1 expression. CD3, CD5 and CD10 were negative. Thorough clinical and imaging investigation showed no evidence of extra- urinary disease. The diagnosis of PMLUB was concluded.
Conclusion: PMLUB represents a rare malignancy with excellent prognosis if detected in an early stage.

PS-08-049

Interfollicular Hodgkin's lymphoma: A diagnostic dilemma

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Objective: Interfollicular Hodgkin's lymphoma represents an unusual pattern of focal involvement of interfollicular zones by Hodgkin's lymphoma along with florid reactive follicular hyperplasia. It is often mistakenly diagnosed as a reactive change. The importance of this pattern of lymph node involvement by Hodgkin's disease rests on its misdiagnosis as a benign lesion.
Method: Three cases of interfollicular Hodgkin's disease were diagnosed in a period of 2 years. All the patients were less than 20 years and all had localised lymphadenopathy. The 3 cases studied did not appear to differ clinically from other recognizable forms of hodgkin's disease.
Results: Lymph node biopsy showed follicular hyperplasia with expanded interfollicular area. Careful search of the interfollicular area showed infiltration by inflammatory cells and scattered Reed-Sternberg and Hodgkin's cells. Immunohistochemistry with CD 15 and CD 30 highlighted the atypical cells.
Conclusion: Recognition of interfollicular Hodgkin's lymphoma is difficult, increasing awareness and a careful examination of the expanded interfollicular areas for Reed - Sternberg cells often clinches the diagnosis. Ancillary support of Immunohistochemical staining for CD15 and CD30 marker is beneficial.

PS-08-051

Primary diffuse large B-cell lymphoma of the ovary: A case report

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Objective: A 35-year-old woman, gravida 2, para 2, was admitted to the hospital with complaints of right, lower abdominal back pain. Abdominal ultrasonography revealed large heterogeneous solid mass at right adnexal region. Patient underwent for right salpingo-oophorectomy and the specimen was submitted for frozen histopathological examination was malignant. The specimen from the left ovarium was also malignant. A gross mass was present in the meso-appendix. Type 1 hysterectomy bilateral salpingo-oophorectomy, retroperitoneal lymph node dissection (RPLND), omentectomy and appendectomy was performed.
Method: The slides were evaluated using hematoxylin-eosin and immunohistochemical staining.

Results: Microscopically, HE stained sections revealed diffuse growth pattern of tumour cells with large vesicular nuclei and prominent nucleoli. There was increased mitotic activity. Tumour cells showed strong staining for CD20 and CD10. Bcl 2 and Bcl 6 show wide moderate immunreactivity. CD3, CD5, cyclin D1, CD30 and TdT were negative for. The high Ki-67 proliferation index was detected %97. These findings revealed diffuse large B-Cell lymphoma. The patient was evaluated post-operatively with bone marrow aspirates and trephine biopsy ruled out any marrow involvement. Follow-up FDG-PET(CT) scans revealed no recurrence for 2 years after therapy.
Conclusion: Primary ovarian lymphoma is rare but it should be considered in the differential diagnosis of a pelvic mass.

PS-08-052
Unusual features of chronic myelogenous leukemia
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Objective: Chronic myelogenous leukaemia (CML) is a myoeloproliferative neoplasm which originates in a bone marrow pluripotent stem cell and is in most cases associated with the BCR-ABL1 fusion gene, which results from translocation between chromosomes 9 and 22 (Philadelphia chromosome). Untreated CML typically develops in three phases - a chronic phase, followed by accelerated and blastic phases. Up to 30 % cases of CML present with mild (MF2) or moderate (MF3) fibrosis, but severe fibrosis (MF3) is rare. We report 2 cases of CML with atypical histopathological features at presentation, including clustering of dysplastic megakaryocytes and osteosclerosis mimicking primary myelofibrosis.
Method: Routine histopathological and immunohistochemical examination of trephine biopsy samples.
Results: Histological examination of two bone marrow samples revealed extreme proliferation of significantly dysplastic clustering megakaryocytes with marked osteomyelosclerosis. Granulocytes were increased, particularly eosinophils. Erythropoiesis was reduced. Blasts were not increased. The morphology was compatible with the diagnosis of primary myelofibrosis. Subsequently performed tests for the BCR-ABL fusion gene were positive in both cases, whereas JAK2617F tests were negative. Acording to clinical, histopathological and genetical findings the diagnosis of CML was established.
Conclusion: Chronic myelogenous leukemia can rarely imitate primary myelofibrosis and may lead to misdiagnosis. To establish an accurate diagnosis it is necessary to corerlate clinical, histopathological and genetic results.

PS-08-053
Nasal extranodal natural killer / T-cell lymphoma: Six case reports
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Objective: Extranodal natural killer (NK)/T-cell lymphoma is an aggressive malignant tumour with distinctive clinicopathological features, characterized by vascular invasion and destruction, prominent necrosis, cytotoxic lymphocyte phenotype and a strong association with Epstein-Barr virus. Most common location is upper aerodigestive tract (nasal cavity, nasopharynx, paranasal sinuses, palate). Presenting symptoms often include nasal obstruction, rhinorrhea, epistaxis, and ulcer of the palate. This is a very rare entity with poor prognosis.
Method: Here was reported 6 cases of extranodal natural killer (NK)/T-cell lymphoma, nasal type, presented history of nasal obstruction and ulcer of the palate. The patients' age range was 29–62 (median: 49,6 year) (2 female, 4 male). Mass in the nasal cavity in five cases and ulcer of the hard in a case palate were revealed in physical examination.
Results: Microscopically, atypical lymphoid cells (large and small) with abundant pale or clear cytoplasm, irregular nuclear borders and immunoblasts, granular chromatin, vesicular nuclei in large cells, inconspicuous nucleoli were seen. Angiocentric and angioinvasive pattern with extensive coagulative necrosis and apoptosis were found. CD3, cytoplasmic, CD56, TIA1, granzyme B, CD4, CD5, CD7 were positive, CD30 was focal positive. They were reported as ENKTCL. Radiotherapy and chemotherapy were performed and the patient was called follow-up.
Conclusion: Extranodal NK/T cell lymphoma is discussed with clinical, radiological, and histopatological findings with literture review. Awareness of this entity will minimize the risk of a misdiagnosis.

PS-08-055
A case of T-cell large granular lymphocytic leukemia
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Objective: T-cell large granular lymphocyte leukemia (T-LGL) is a rare disorder characterized by clonal proliferation of cytotoxic T-cells in the peripheral blood (PB) and bone marrow (BM).
Method: A 62-year-old woman came to the hospital with a 3-month history of breathlessness and edema.
Results: Her complete blood count indicated transfusion-dependent anemia and lymphocytosis but platelet count was normal. On her PB smear, lymphocytes containing multiple granules was found, with a median diameter of 13 μm, smaller than typical LGL tumour cells. Flow cytometry of PB showed tumour cells were CD 8+ T-cell, and clonal rearrangement of the TCR gene was detected, suggested the diagnosis of T-LGL. On her bone marrow biopsy, the original structure was preserved and the tumour cell cluster was difficult to identify. Additional immunohistochemical analysis for cell block preparation of PB revealed the tumour cell positivity of cytotoxic molecules.
Conclusion: Although the observed cell size was smaller than typical LGL tumour cells, PB smear morphology, immunophenotype, and clonal rearrangement of the TCR gene suggested the diagnosis of T-LGL. LGL is an indolent hematopoietic neoplasm but have low prevalence, immunohistochemistry and PB examination are helpful to make the diagnosis.

PS-08-057
Experience of two centers' histopathological and immunhistochemical characteristics of Hodgkin's lymphomas in mediterranean Turkey
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Objective: Clinical, histopathological and immunohistochemical characteristics of Hodgkin's lymphoma (HL) was investigated in Mediterranean of in Turkey.
Method: One hundred thirty seven cases that had been diagnosed as HL and of which complete clinical and histopathological information could be fully accessed at two hospital clinics.
Results: The average age of the subjects was 28.84 years. The distribution of the ages of these cases, in terms of decades, was 13.1% in the first decade, 24.8 % in the second decade, 20.4 %in the third decade, 8.7 % in the fourth decade and 13 in the fifth or a subsequent decade. There were 89 males and 48 females. There were 3 cases of nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) and 134cases of classical Hodgkin lymphoma. All tumours were stained for CD30, CD15,CD20,CD3.CD30 was expressed in 134cases (100 %), CD20 was expressed in 33 cases (24.6 %) with different level of intensity. CD3was not expressed. CD15 staining was performed in 13 cases and 88 (65.6 %) cases were positive. The most frequent localisation site was cervical region(48.9 %). The most frequent symptom was pain-free

lymphadenopathy (80.2 %). With respect to the histological sub-types, nearly every case was classical HL, 34.3 % of the cases were identified as having the mixed cellular type, 60.4 % had the nodular sclerosing type, 3.7 % had the lymphocyte rich type 1.4 % had th lymphocyte depleted type. Bone marrow involvement was 10.2 %.
Conclusion: Our epidemiological data are generally compatible with data from both underdeveloped and developing countries. The results of immunohistochemical staining that we have obtained in this study are in line with the literature data.

PS-08-060
Primary cutaneous acral CD8+ T cell lymphoma: A new entity and a rare case report
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Objective: Primary cutaneous acral CD8+ T cell lymphoma is a rare tumour which has been described as a new indolent provisional entity, originally described as originating in the ear. There has been described in nose in a few cases. We present a case which has an indolent course in nose.
Method: Microscopy and immunohistochemical stains were applied.
Results: A 56 years old man, presented with a wound on his nose since 2014. He has had some different diagnosis until this time, such as lupus vulgaris, squamous cell carcinoma and T cell lymphoid hyperplasia. His wound has not healed and a partial rhinectomy has applied. Microscopy revealed a dense, diffuse lymphoid infiltration in dermis that consisted of CD3+, CD8+, CD7+, TIA-1 + and granzyme + small/medium sized lymphocytes. Atypical lymphoid infiltration also showed invasion in the vessel wall and cartilage. There was focal necrosis in some areas. Primary cutaneous acral CD8+ T cell lymphoma was diagnosed according to histopathologic and immunohistochemical findings.
Conclusion: Primary cutaneous acral CD8+ T cell lymphoma is a rare tumour and is new entity. Primary cutaneous acral CD8+ T cell lymphoma is a rare tumour and a new entity. The lesions are nearly always localized to a single site and therefore can be managed conservatively. It's important to know and remember this diagnosis because of the treatment is unique.

PS-08-061
Investigation the presence of Epstein-Bar virus in diffuse large B-cell lymphoma
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Objective: Epstein-Bar Virus (EBV) positive diffuse large B cell lymphoma (DBLCL) is a new category in 2016 World Health Classification of lymphoid neoplasms and it has been increasingly recognized in younger patients and better survival
Method: 61 patients with DLBCL has been included in this study. We grouped with patients according to their ages as under 50 and above 50. We used EBV coded RNA (EBER) chromogenic in situ hybridization method to determine EBV in these cases. We also studied bcl-2, bcl-6 and c-myc immunohistochemistry to these cases. EBER expression was specified as positive/negative. Bcl-2, bcl-6 and c-myc expressions were grouped as their percentages.
Results: Sixteen of patients were under 50 years old and 45 of them were above. EBER expression were seen in 4 patients and 3 of them under 50 years old.
Conclusion: EBV positive DLBCL can be seen in the young age group. We suggest that EBER should be assessed in all ages in DLBCL. There will be an opportunity to study and and develop targeted therapy in the management of patients with EBV positive DLBCL.

Monday, 4 September 2017, 09:30–10:30, Hall 3
PS-09 Head and Neck Pathology

PS-09-001
Neuroendocrine carcinomas of head and neck: Review of cases in La Paz Hospital since 1965
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Objective: To review the neuroendocrine carcinomas (NEC) of head and neck.
Method: We searched and reviewed the NEC of head and neck area diagnosed in La Paz Hospital since 1965.
Results: We found 7 cases of NEC. Four in the salivary gland (3 in the parotid and 1 in the submandibular gland), 2 in the larynx and 1 in the oropharynx. Five were small cell NEC (SCNEC) and 2 large cell NEC (LCNEC). The salivary gland carcinomas did not have metastasis but 1 patient died of the disease. Both laryngeal carcinomas had hepatic and bone metastasis and died. The most recent patient is a 62-year-old woman who presented with a mass in the right tonsil and uvula. She presented with metastasis to the regional lymph nodes. She is being treated with chemotherapy.
Conclusion: NEC in head and neck localisation are extremely rare. In our series, the most common site of presentation was the salivary gland followed by the larynx. They were all poorly differentiated tumours. All of them were tested to exclude metastasis from other sites. The salivary gland NEC presented without metastasis and seem to have a better prognosis.

PS-09-002
Case report: Hyalinising clear cell carcinoma
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Objective: Hyalinizing clear cell carcinoma (HCCC) is a rare, low grade salivary gland carcinoma with excellent prognosis. It must be distinguished from carcinomas with myoepithelial differentiation, squamous cell carcinoma (SCC) and mucoepidermoid carcinoma (MEC). We report a case of a 59-year-old male with HCCC of minor salivary gland. The pre-excision biopsy sample from the tumour located at the root of the tounge and the lateral wall of the pharynx was diagnosed as basaloid SCC. Examining the tumour after complete resection lead to the diagnosis of HCCC.
Method: The tissue samples from the tumour were embedded in paraffin; the slides were examined by light microscopy. P63, S100, panCK, CK7, CK5, CK14, SMA, CD10, WT1, calponin, p16 immunohistochemistry was performed. Fluorescence in situ hybridization (FISH) was used to detect EWSR1 gene translocation. Periodic acid-Schiff (PAS) stain was also carried out.
Results: The tumour cells were positive for p63, panCK, CK7, CK5 and CK14. S100, SMA, CD10, WT1, calponin, p16 were negative. EWSR1 translocation was confirmed using FISH.
Conclusion: We present a rare salivary gland carcinoma. Our case showed similar morphologic features and immunohistochemical profile to myoepithelial carcinoma. Detection of EWSR1 gene re-arrangement helped to separate HCCC from its histological mimics.

PS-09-003

Clinicopathological spectrum of Warthin tumour in a Tertiary Cancer Referral Center

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Objective: Warthin tumour (WT) is the second most common benign tumour of the parotid gland with a variable clinical presentation including substantial number of cases detected incidentally. This study aimed at review of clinicopathological spectrum of WT in a tertiary cancer center over a 10-year period.
Method: Slides of cases diagnosed as WT at our institute in last 10 years were retrieved from the archives and reviewed. The clinical details were obtained from the electronic medical records.
Results: A total of 33 cases were identified (32 males, 1 female; age 42–87 years). The clinical presentation at the time of diagnosis was: parotid swelling (14 cases), cervical swelling (8 cases), incidentally detected (8 cases), while the presentation was not known in 3 cases. On histopathological review, four cases (12.1 %) were multifocal (two bilateral, two unilateral). Fourteen of these cases (42.4 %) were associated with other malignancies, of which three (9.1 %) were associated with salivary gland malignancy. Eleven cases (33.3 %) were associated with other malignancies, one of them being carcinoma of unknown primary with widespread metastases.
Conclusion: Higher incidence of WT associated with other malignancies was noted in our series, which can be explained by cases being referred to tertiary cancer center.

PS-09-004

Case report of a primary thyroid lymphoma and review of the literature

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Objective: Primary thyroid lymphoma (PTL), a rare type of malignant tumour, typically occurs in elderly women with history of thyroiditis (lymphocytic thyroiditis/Hashimoto's thyroiditis-HT). Epidemiological studies have shown increased risk for developing lymphoma in the setting of autoimmune disorders. Thus, early diagnosis requires awareness of increased index of suspicion of PTL in patients with HT.
Method: A 61 year old woman with 10 years history of HT was referred to our institution with recent enlargement of the right thyroid lobe in ultrasonography.
Results: Histologic examination revealed a MALT-type lymphoma with extensive HT lesions. Immunohistochemistry demonstrated that tumour cells expressed CD20, BCl-2, with monotypic immunoglobulin expression and light-chain restriction. We retrospectively analyzed five more patients with PTL. Patients were all females, with a median age of 70 years. Three different subtypes of lymphoma were observed: Three had diffuse large B cell lymphoma (DLBCL), one had MALT-type lymphoma and one had Burkitt's lymphoma. TH was observed in three patients.
Conclusion: One of the differential diagnosis of a rapidly growing large thyroid mass in elderly persons with history of HT is PTL. Our report emphasizes the need for clinical awareness in such cases.

PS-09-005

The value of convential histopathological criteria for the stratification of clinical behaviour and prognosis of the oral squamous cell carcinoma

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Objective: The aim of our study was to evaluate the clinical and histopathological criteria of oral squamous cell carcinoma.
Method: The 35 patients were retrospectively enrolled in the study. The histopathological and clinical data were retrospectively evaluated. Histopathological characteristics were correlated with clinical data. Statistical analysis was performed by GraphPadPrism 7.0 version software. The p value < 0.05 was considered as statistical significant.
Results: Obtained results stowed that the average patients' age was 57,34 ± 8,142 years (range = 39–78). Predominantly the tumours were moderately differentiated. The average tumour size was 2.171 ± 1.302 cm. Obtained results showed that the nine patients (25.7 %) had tumour recurrence. The negative correlation between metastasis in lymph nodes (N stage) and stromal lymphocytic infiltration was observed ($r = -0.37$; $p = 0.03$). In addition, the negative correlation between tumour invasion in lymphatic vessels and stromal lymphocytic infiltration ($r = -0.37$; $p = 0.03$) was revealed. The positive correlation N stage and tumour lymphatic invasion was demonstrated. Furthermore, the positive correlation between lymphatic invasion and tumour size was observed. In addition, the positive correlation between perineural invasion and stromal desmoplasia was revealed (respectively $r = 0.37$, $p = 0.02$).
Conclusion: The assessment of histopathological criteria is important for the stratification of clinical behaviour and prognosis of the oral squamous cell carcinoma.

PS-09-006

Head and neck tumours - a two and a half year study in a Romanian Pathology Institute

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Objective: Worldwide, head and neck cancer accounts for more than 550,000 cases, males/females ratio ranging from 2:1 to 4:1. The most common sites are the larynx, oral cavity and oropharynx and more than 90 % of the tumours are squamous cell (epidermoid) carcinomas, adenocarcinomas, sarcomas and lymphomas.
Method: We present a study made on head and neck tumours during two and half years which diagnosis was made using histological and immunohistological metods.IBM SPSS Statistics version 20.0 (SPSS Inc., Chicago, Illinois, USA) was used for data analysis.
Results: We studied head and neck tumours from 93 pacients, 50 males and 43 females, with age variations from 3 to 83 years old. 83 tumours were primitive and the rest were metastasis. The most affected region was the parotid gland, the main type of benign tumour was pleomorphic adenoma and the most frequent malignant tumour was lymphoma. The metastases were mostly adenocarcinomas with primitive tumours in organs such as breast, colon and lung. The variables we've studied had no statistical semnificance.
Conclusion: In our study, head and neck tumours remain a main cause of cancer in males, frequent in the parotid gland, most as primitive tumours. Lymphomas and non-keratinizing squamous cell carcinoma are the most encountered diagnoses.

PS-09-007

Sclerosing polycystic adenosis: A rare tumour of the salivary glands

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Objective: Sclerosing polycystic adenosis (SPA) of salivary glands is a rare lesion of undefined nature. About 80 % of SPA cases occur in the parotid gland. We report a case of SPA in order to emphasize its clinicohistological features and to discuss its differential diagnoses.
Method: The histological features of SPA of the parotid are described with a review of the related literature.

Results: An 11-year-old girl presented with a painful left-sided parotid mass. A fine needle aspiration suggested a Warthin's tumour. A parotidectomy was performed. Gross examination revealed an unencapsulated 3 cm mass. Histologically, the mass was composed of acinar and ductal components with a lobular architecture. Acinar cells had eosinophilic cytoplasmic zymogen granules and focally a sebocyte-like appearance. Ducts varied in size from ductules to cystically dilated spaces and showed foci of epithelial hyperplasia. All these components were embedded in a dense sclerotic collagenous stroma. There was no recurrence at 9 months of follow up.
Conclusion: SPA of the salivary glands is an under-recognized lesion which may be confused with other types of salivary gland tumours. It is considered benign, however epithelial atypia are commonly observed. A complete surgical resection and a long-time follow up are required in order to prevent a local recurrence.

PS-09-008
A rare case of pure nasopharyngeal carcinoma in situ
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Objective: Pure nasopharyngeal dysplasia or carcinoma in situ have rarely been documented.The prevalance of nasopharyngeal carcinoma in situ was reported to be 3−8 % in biopsies of nasopharyngeal carcinoma. In most cases, in situ component was adjacent to invasive carcinoma. We present a case of pure nasopharyngeal carcinoma in situ without accompanying invasive component or subsequent development of invasive carcinoma in follow-up period.
Method: In August 2012, a 56 year-old patient's nasopharyngeal biopsy consultation has been made to our institution. At histologic examination surface epithelium showed severe dysplasia without invasion. A month later, nasopharyngeal endoscopy was performed and multiple biopsies were taken. Biopsies revealed severe cytological atypia affecting the whole thickness of the epithelium without invasion and reported as carcinoma in situ. A month later at another endoscopy, nasopharynx looked normal and histologically focal dyplasia was seen.
Results: The patient was treated with radiotherapy. At patient's follow up endoscopies, nasopharynx looked normal and no pathological findings were detected on biopsy specimens.
Conclusion: Although natural history of pure nasopharyngeal carcinoma in situ is not fully understood, it is well documented that a proportion of patients develop invasive carcinoma on follow-up. For this reason, careful histopathological examination of nasopharyngeal surface epithelium is crucial for detecting such precursor lesions.

PS-09-009
The use of CD 105 as a marker of mast cell
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Objective: The aim of this study was to evaluate the use of CD105 as a biological marker of mast cells compared with the gold standard stain
Method: This study consisted of 15 cases of neurofibroma, 09 cases of mastocytoma and 06 cases of fibrous scar tissue. Immunohistochemistry was performed for CD 105 and Mast Cell Tryptase as well as histochemical staining using Toluidine Blue for the identification of mast cells. Quantitative analysis of the cells was performed by counting 5 hotspots at 20x magnification. The validity of CD 105 as a mast cell marker for mastocytoma, neurofibroma and scar was assessed by intraclass correlation coefficient (ICC) calculations according to Fleiss's classification. The Kruskal-Wallis test was used to compare mast cell count in mastocytoma, neurofibroma and scar tissue for each marker.
Results: A strong CD105 expression was found in the cytoplasmic granules of mast cells from all groups. Similar results were observed with mast cell tryptase as well as toluidine blue. The ICC revealed that CD105 is a highly reliable biomarker of mast cells when compared to mast cell tryptase and toluidine blue in neurofibromas, mastocytoma and fibrous scar tissue.
Conclusion: This study suggests that CD105 could be a good marker of mast cells.

PS-09-010
Review of 101 benign epithelial, mesenchymal and mixed odontogenic tumours
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Objective: Odontogenic tumours are a group of rare and heterogenous lesions showing divergent epithelial and/or mesenchymal elements. Odontomas are the most common tumours however the frequency and gender predilection of cases show geographic variation.
Method: We reviewed 101 cases diagnosed between 2000 and 2016, and compared by non-parametric tests.
Results: Most common diagnostic group were epithelial (60.4 %) followed by mesenchymal (22.8 %) and mixed epithelial-mesenchymal tumours (18.8 %). Ameloblastoma was the most frequent tumour (57.4 %) followed by odontoma (14.9 %) and odontogenic myxoma/myxofibroma (11.9 %). Mandible localisation was 4 times higher. Two cases of cemento-ossifying fibroma were located sphenoethmoid sinuses. Mesenchymal and mixed tumours were seen in females ($p = 0.012$), while ameloblastomas were distributed equally among both sexes ($p = 0.05$). The frequency, median age and gender (male:female) distribution of the cases were as follows; Ameloblastoma (57.4 %, 40 ± 18.5 y.o M/F: 30/28), odontoma (14.9 %, 19 ± 19,M/F: 4/11), odontogenic myxoma/myxofibroma (11.9 %, 22 ± 16, M/F: 4/8), cementossifying-fibrom (%5,34 ± 12,all female), cementoblastom (5 %, 23 ± 9,all female), adenomatoid odontogenic tumour (3 %, 24 ± 3,all female), ameloblastic fibroma (2 %, 28 ± 9,both female), odontogenic fibrom (1 %, 59 y.o, female).
Conclusion: Ameloblastoma was the most frequent tumour, similar to Asian, African and Indian series followed by odontoma while frequency of adenomatoid odontogenic tumour was lower than Indian series. Age distribution was similar to literature despite more frequent female predilection.

PS-09-011
Alveolar rhabdomyosarcoma with multiple metastases: A case report
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Objective: Alveolar rhabdomyosarcoma is a soft tissue tumour located in the head and neck region which is common in childhood. It is a highly aggressive round-cell tumour partially showing skeletal muscle differentiation.
Method: A 40-year-old male patient presented to the hospital with swelling on the right side of his neck. Magnetic resonance imaging showed a destructive, 5 cm soft tissue mass filling the maxillary sinus and expanding into the orbital cavity. The cause of the initial symptom which was swelling on the neck turned out to be because of multiple metastases to the lymph nodes. As the symptoms developed rapidly, the patient suffered from blurred vision and proptosis of the right eye.
Results: The microscopical examination of the biopsy specimen revealed cells that were variable in size and shape with eosinophilic narrow cytoplasm and hyperchromatic nuclei. Mitotic figures were evident. Immunohistochemistry panel including epithelial, mesenchymal and lymphoid markers supported the diagnosis of an alveolar rhabdomyosarcoma.

Although chemotherapy had been started, the patient died due to rapid and wide metastatic spread of the tumour to axilla, bone marrow and pancreas.
Conclusion: This case of sinonasal alveolar rhabdomyosarcoma is presented not only for its relatively rare primary site but also for a number of unusual metastases leading to death in a short time.

PS-09-012
HBME1 relevance for salivary gland Warthin tumour histogenesis
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Objective: The histogenesis of Warthin tumours (WT) whether true neoplasm or hyperplasia, is matter of debate. The aims of our study were to assess the expression of the HBME1 antigen in parotid WT and the relationships to CK5/6, P63 and WT1 expression.
Method: Four parotid WTs (and surrounding parotid) were studied by immunohistochemistry for HBME1, CK5/6, P63 and WT1 expression.
Results: Membrane and/or cytoplasmic HBME1 were observed in a focal distribution, in luminal and suprabasal epithelial cells of all WTs. Cytokeratin 5/6 as well as P63 were expressed in a continuous pattern, in basal and focally suprabasal cells. WT1 was expressed focally at the luminal border of ¾ WTs. In the nontumoural parotid, HBME1 was expressed in ductal/luminal cells of intercalated ducts and interlobular ducts, mainly in a diffuse pattern while CK5/6 and P63 in the basal myoepithelial cells.
Conclusion: The expression patterns we have observed for HBME1 are consistent with an origin of the Warthin tumour epithelium from the intercalated and/or interlobular salivary gland duct epithelium. The immunohistochemical profile HBME1 + CK5/6 + P63+ in the WT epithelium parallels rather that of mesothelioma/metaplastic mesothelial cells, than that of thyroid carcinomas (showing only rarely CK5/6 and/or P63 positivity), suggesting a primordial coelomic phenotype/differentiation.

PS-09-013
Cytokeratin 7 expression in neck metastasis of primary oropharyngeal squamous cell carcinomas (SCC): Could this be a useful biomarker in locating primary tumours to tonsils?
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Objective: Cystic nodal metastases in the neck have been shown to be associated with HPV related primary tumours, the majority of which in this region arise in the oropharynx (OP). The link between CK7, as a marker of junctional sites including the oropharynx, and HPV is the focus of ongoing investigation. The aim of this study is to investigate CK7 expression in neck node metastases from OP primaries, to determine the relationship between CK7 expression and the development of cystic metastases, tonsil subsite, p16 expression and HPV detection.
Method: Forty seven nodal metastases from primary OPSCCs were evaluated for CK7 expression by IHC and results correlated with p16 expression, HPV status by ISH and PCR techniques, tumour subsite within the oropharynx and the presence of cystic nodal metastases. The sensitivity and specificity of HPV ISH and p16 IHC was compared with HPV PCR.
Results: CK7 expression in lymph node metastases from OPSCCs significantly correlated with HPV detection but not with p16 expression. CK7 expression was not significantly related to cystic metastases as it was also expressed in noncystic metastases. CK7 was expressed in metastatic nodes associated with a primary tonsillar SCC, but was not expressed in metastases from soft palate or posterior pharynx primaries.
Conclusion: When considering OPSCCs, CK7 expression in lymph node metastases remains a significant predictor of a HPV related primary tumour. This finding was regardless of the cystic nature of the metastasis. The expression of CK7 was only found in lymph node metastases from tonsillar tumours, which could signify the predictive value of this marker in relation to primaries of tonsillar specific origin.

PS-09-014
Molecular characterisation of sinunasal carcinomas
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Objective: To identify genomic alterations (GA) in sinonasal carcinomas
Method: Next generation sequencing (Illumina MiSeq reagent Kit V2) targeting 17 genes, FISH (ZytolightSPEC MYB/NFIB) and immunohistochemistry were performed on 37 squamous cell carcinomas (SCC), 15 inverted papillomas (IP), 12 adenocarcinomas (AC), 1 adenosquamous carcinoma (ASC), 5 adenoid cystic carcinomas (ACC) and 5 undifferentiated carcinomas (SNUC) of sinonasal cavities.
Results: EGFR exon 20 mutations were more common in IP (94 %) and SCC arising from IP (75 %) than in other histologic subtypes (p = 0.000001). ERBB2 p.A771_M774dup mutation was detected in one IP. TP53 mutations were detected in SNSCC-associated IP and associated SNSCC (83 %) but in none of simple IP, indicating that TP53 mutations are acquired at a later stage in tumourigenesis than mutations in EGFR/ERBB2. KRAS mutations were observed in one AC of intestinal type (p.G12V), one SCC (p.G12D) and one ASC (p.G12D). Other frequent mutations were found in NFE2L2, PTEN and PIK3CA. MYB-NFIB fusion was identified in ACC as it is also described in ACC of the oral cavity and the breast. SNUC shows no recurrent mutation in comparison to other histotypes.
Conclusion: Our analysis demonstrates that different histotypes of sinonasal carcinomas show different typical GAs. Further studies are mandatory to investigate the clinical significance.

PS-09-015
Adenoid cystic carcinoma (ACC) of the larynx: Inmmunophenotypical and clinicopathological study of eight cases from a single institution
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Objective: Laryngeal ACC is a rare malignant tumour originating from minor salivary glands of the larynx. We report the immunophenotypical and clinicopathological features of eight more cases.
Method: Cases of laryngeal ACC diagnosed and treated at Vittorio Veneto Hospital were retrieved. Slides, paraffin blocks and clinical records were collected and reviewed. A panel of immunostains was applied, including Smooth Muscle Actin, S100 protein, Cytokeratin AE1-AE3, CD117, MYB and Epithelial Membrane Antigen.
Results: Six patients were female and two male, with an age range at diagnosis of 25−62 years (median 43). The subglottis was involved in five cases and supraglottis in three. Different treatments were used according to tumour extension: total laryngectomy in 3 advanced cases and partial resection in the rest. Follow-up was available in 7 cases and ranged 9–216 months (median 36): local regional nodes metastasis at presentation occurred in one, late local recurrence occurred in another one, the rest were alive with no evident disease.
Conclusion: Laryngeal ACC is a rare disease. Partial resection in clinically limited tumours seems advisable. Large multi-institutional are needed to better knowledge and optimize treatment of such rare entities.

PS-09-016

Contribution of the miRNA expression profile for the identification of the anatomic location of squamous cell carcinoma of the lung and head & neck

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Objective: The determine and differentiate the lung carcinoma whether it is a primary or metastasis in a patient with history of head and neck squamous cell carcinomas (HNSCC) can be challenging even after pathologic, clinic and radiologic assessment. The aim of this study was determine the relation of miRNA expression alteration with anatomic localisation of tumours
Method: In total, 40 patients with HNSCC and 10 patients with Lung squamous cell carcinoma (SCC) were enrolled in present retrospective study. Formalinfixed paraffin embedded (FFPE) samples were sectioned and deparaffinized, and total RNA was isolated. mir-9, mir-126, mir-182, mir-191 and mir-486 expressions were analyzed with Taqman assay by qRT- PCR.
Results: We found a significant difference in expression levels of mir-9, mir-126, mir-182 and mir-486 between HNSCC and Lung SCC ($p < 0,05$). The expression level of mir-486 was down-regulated in lung and laryngeal SCC and overexpressed in hypopharyngeal and oral SCC. The expression levels of mir-126 was down-regulated in all localisations and the down-regulation was more significant in lung SCS ($p < 0,05$). When the mir-126 and mir-486 were used as a dual panel; lung SCC can be differed from hypopharynx and oral cavity-derived SCC by 100 % sensitivity and specificity (AUROC: 1,0). The distinction of lung SCC from laryngeal SCC can be evaluated with expression level of mir-126 (AUROC: 1,0).
Conclusion: Although there is still no biomarker to distinguish origin of the lung SCC in a patient with history of HNSCC, comparison of miRNA expression alterations may be useful.

PS-09-018

Minor salivary gland biopsy diagnoses in patients with Sjögren's syndrome and anti-Ro antibodies

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Objective: To determine the diagnostic categories on minor salivary gland biopsy (MSGB) in a consecutive series of patients with Sjögren's syndrome (SS) with anti-Ro antibodies, correlating them with age and duration of xerostomy.
Method: Subjects: 44 consecutive patients meeting American-European-Consensus-Group criteria for SS with anti-Ro antibodies and MSGB diagnosed between 2014 and 2016. Method: retrospective observational study and statistical analysis (Mann-Whitney test). Variables: age at diagnosis; duration of xerostomy previous to diagnosis; histopathological diagnosis according to Daniels' categories.
Results: Median of age at diagnosis is 57,5 years, and median of duration of xerostomy 36 months. 36′4 % of cases show Focal Lymphocytic Sialoadenitis (FLS) with focus score (FS) ≥ 1; 18,2 % Focal/Sclerosing Lymphocytic Sialoadenitis (F/SLS) with FS ≥ 1; 18,2 % Sclerosing Chronic Sialoadenitis (SCS); 11,4 % FLS with FS < 1; 13,6 % Nonspecific Chronic Sialoadenitis; and 2′3 % normal gland. Duration of xerostomy is higher in SCS versus the group with FS ≥ 1 (FLS and F/SLS), and patients are older in the cases with fibrosis (F/SLS and SCS) versus FLS with FS ≥1, with statistical significance ($p = 0,02$ and $p = 0,019$ respectively).
Conclusion: MSGB in patients with SS can present variable histopathological findings, some including fibrosis, what seems related to time of evolution and age and can limit its diagnostic value in older patients.

PS-09-019

Immuno-metabolic determinants of chemoradiotherapy response and survival in head and neck squamous cell carcinoma (SCC)

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Objective: Tumour immune microenvironment and tumourmetabolism are major determinants of chemoradiotherapy response. We assessed the interdependency and prognostic significance of immune and metabolic phenotypes in head and neck cancer (HNSCC) and evaluated reactive oxygen species (ROS) changes as a mechanism of treatment response in tumour spheroid/immunocyte co-cultures.
Method: Pretreatment biopsies were immunohistochemically characterized in 73 HNSCC patients treated by definitive chemoradiotherapy and correlated with survival. The prognostic significance of CD8A, GLUT1 and COX5B gene expression were analyzed within The Cancer Genome Atlas (TCGA) database. HNSCC spheroids were co-cultured with peripheral blood mononuclear cells (PBMC) in the presence of the glycolysis inhibitor 2-Deoxyglucose (DGL) and radiation treatment followed by PBMC chemotaxis determination via fluorescence microscopy.
Results: In chemoradiotherapy-treated HNSCC mitochondrial-rich (COX5B) metabolism correlated with increased and glucose-dependent (GLUT1) metabolism with decreased intratumoural CD8/CD4 ratios. High CD8/CD4 together with mitochondrial-rich or glucose-independent metabolism was associated with improved short-term survival. TCGA analysis confirmed that patients with a favorable immune and metabolic gene signature had improved short- and long-term survival. In vitro, DGL and radiation synergistically upregulated ROS-dependent PBMC chemotaxis to HNSCC spheroids.
Conclusion: Our results suggest that glucose-independent tumourmetabolism is associated with CD8-dominant anti-tumour immune infiltrate, and together these contribute to improved chemoradiotherapy response in HNSCC.

PS-09-022

Questioning the role of p16 as surrogate marker for Human papillomavirus (HPV) driven head and neck cancer

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Objective: The awareness on the role of Human papillomavirus (HPV) as driver for oropharyngeal squamous cell cancer (OPSCC) and as critical indicator for disease outcome increases and p16 Protein expression is widely used as surrogate marker. However, it may not suffice. We assessed whether p16 overexpression in non-keratinizing tumours, as recommended by the College of American Pathologists, is an adequate marker for HPV presence.
Method: In a cohort of over 150 patients with OPSCC, including a subset of cases without prior p16 testing, diagnosed at our institute we assessed p16 expression, keratinization and HPV status. For molecular HPV detection the VisionArray system by ZytoVision was used.
Results: By comprehensive analysis we found a significant number of discrepant cases. Twenty percent of p16 positive tumours were HPV negative in the molecular test, among them a considerable number of non-keratinizing cancers. Furthermore, we could identify clearly keratinizing carcinomas which turned out to be HPV positive.
Conclusion: Based on our results we conclude that using p16 as surrogate marker, with or without morphologic features, for HPV driven OPSCC bears the risk of incorrect tumour classification, false prognostication and both over- and undertreatment of patients. Direct molecular HPV testing can help to avoid misdiagnoses.

PS-09-024

Establishment and characterisation of primary oral squamous cell carcinoma (SCC) cell lines from Iranian population by enzymatic method and explant culture

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Objective: Oral Squamous Cell Carcinoma (OSCC) is the most frequent oral cavity cancer. It is known as the eight most common cancers in men and the fifth in women. Various prevalence of this cancer has been reported throughout the world, in terms of geographical regions.

Method: Tissue samples were obtained from oral cancer patients and enzymatic, explant culture and MACS methods were used for isolation cells. After confirmation of quality controls, characterization and authentication of OSCC cells were determined by STR, Chromosome analysis, Species identification, monitoring the growth, morphology, expression of CD326 and CD133 markers.

Results: We have successfully established a total number of five Iranian OSCC cell lines.

Conclusion: Regarding the data obtained from the current study, it can be inferred that these cell lines will provide an extremely useful platform for studying carcinogenesis pathways of OSCC in Iranian population and may explain the ethnic differences and anti-cancer drug response in upcoming studies.

PS-09-026

SMARCB1 (INI1)-deficient sinonasal clear cell carcinoma (CCC): A new histological variant

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Objective: SMARCB1-deficient sinonasal carcinoma with clear cell morphology, a new variant.

Method: Case report.

Results: A 43 year old male presented with blurred vision and headaches. CT & MRI revealed a left sphenoid/ethmoid sinus mass. A biopsy showed a high grade tumour composed of sheets of clear cells without evidence of squamous or glandular differentiation. A minority of cells contained eosinophilic cytoplasmic inclusions imparting a rhabdoid morphology. Immunohistochemically, the tumour cells were positive for AE1/AE3 and CK7 with focal staining for CK5, CK20, calretinin, vimentin and SMA. There was diffuse loss of nuclear staining for INI1. The patient underwent neoadjuvant chemotherapy and craniofacial resection, but died 3 months postoperatively.

Conclusion: SMARCB1-deficient sinonasal carcinoma, a recently described aggressive primary sinonasal malignancy, typically has a basaloid appearance. The predominantly clear cell morphology seen in this case has, to our knowledge, not been described and may cause diagnostic confusion with other clear cell carcinomas. Immunohistochemistry for INI1 loss should be considered when dealing with undifferentiated sinonasal carcinoma, including those with clear cell change. This will facilitate appropriate diagnosis and allow for a more comprehensive understanding of this entity.

PS-09-027

Hedgehog pathway proteins SMO and GLI expression in head and neck squamous cell carcinoma (HNSCC) – a potential therapeutic target?

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Objective: The hedgehog pathway is involved in many cancer types and suitable for targeted therapy. Recent studies showed that the hedgehog pathway might be also a target in head and neck cancer.

Method: We evaluated the hedgehog pathway proteins SMO and GLI as well as p53 expression by immunohistochemistry in 101 patients with squamous cell carcinoma of the head and neck (HNSCC). Correlation with clinico-pathological factors (tumour stage, lymph node status, grading) was performed.

Results: Immunoreactivity for SMO and GLI was found in 36 (35,6 %) and 91 (90 %) of tumours. Positivity of both proteins was found in 35 (34,7 %). Expression of both hedgehog pathway proteins SMO and GLI did not correlate with tumour stage, lymph node status or tumour grade. However, expression of GLI showed statistically significance with positive lymph node status regardless of tumour stage ($p < 0.01$). P53 alteration correlated with higher tumour grade ($p < 0.01$) but not with SMO and GLI expression.

Conclusion: Expression of hedgehog pathway proteins was found in a substantial number of HNSCC. GLI expression significantly correlated with disease progression (lymph node metastases). Targeting the hedgehog pathway in HNSCC might have therapeutic potential and further molecular analyses are needed to elucidate therapeutic options.

PS-09-028

Clear cell carcinoma (CCC): A case report with review of literature

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Objective: Because clear cell carcinoma (CCC) is a low-grade carcinoma, it is very important to recognize it and to distinguish it from other carcinomas « with clear cells », especially the clear cell squamous carcinoma, whose treatment and prognosis are very different.

Method: We present the case of a 43-year-old woman, without any history of cancer, tobacco or alcohol habit, who had for 1 year a retromolar mass, with osseous invasion but without node or hematogeneous metastases. Surgery was performed.

Results: Histologically, this lesion was infiltrative, with solid nests and sheets of large glycogen-rich clear cells and smaller eosinophilic cells, surrounded by a sometimes hyalinized stroma. Atypia were very moderate. Mitoses were rare in the majority of the tumour. Tumour cells were positive for cytokeratine CK5-6 and p63, and negative for myoepithelial markers. The identification of EWSR1 rearrangement by FISH confirmed the diagnosis of CCC.

Conclusion: CCC is a rare tumour of accessory salivary glands characterized by a constant but non specific EWSR1 rearrangement. It occurs in adults, with a slight female predominance, mostly in the oral cavity. Differential diagnoses are discussed with other head and neck tumours « with clear cells », some of them also with EWSR1 rearrangement.

PS-09-030

Prognostic relevance of EGFR expression in laryngeal squamous cell carcinoma (LSCC)

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Objective: The aim of our work is to study the immunohistochemical expression of EGFR in laryngeal squamous cell carcinoma (LSCC) and its correlation with risk factors, tumour location, TNM stage and histological grade.

Method: Our retrospective descriptive study focused on 30 cases of LSCC collected during a period of 6 years from January 2010 to January 2016. A histological examination as well as an immunohistochemical study using the EGFR antibody were performed.

Results: A positive EGFR immunoexpression was encountered in 26 cases (86.7 %, *n* = 26/30). The notion of tobacco was found in all EGFR positive cases (100 %, *n* = 26/26). Alcohol consumption was found in 12 positive EGFR cases (46 %, *n* = 12/26). EGFR immunoexpression was present mainly in cases of glottic localisation (76.92 %, *n* = 20/26). EGFR is most frequently positive in tumours classified T4N0M0 (30.8 %, *n* = 8/26). Regarding tumour grade, immunoreactivity of EGFR was mostly present in 19 cases of grade I tumours (73.2 %, *n* = 19/26). There is only one case of carcinoma in situ. This case was positive for EGFR (3.8 %, *n* = 1/26).
Conclusion: Our study revealed a correlation between the immunoreactivity of EGFR and risk factors, tumour location, TNM stage and histological grade. However its prognostic value remains controversial.

PS-09-031
Effects of chronic alcoholism on dendritic cells of the oral mucosa during wound healing
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Objective: The acute ingestion of ethanol causes the inhibition of dendritic cells (DC) migration and differentiation in skin tissues. However, this effect has not been described in the oral mucosa. This study aimed to verify if chronic alcoholism affects the dendritic cell repopulation during wound healing process.
Method: Immunohistochemistry for CD1a, CD11c, CD207 and vimentin (DC markers) was performed in tissue sections of previously induced wounds in mice, that were divided in Ethanol group (EG) (exposed to ethanol solution during 28 days) and Control group (CG). Immunostaining was assessed 24 hrs, 3, 7 and 9 days after wound induction. Immunostained cells were analyzed quantitatively in conjunctive tissue and epithelium.
Results: The number of immunostained cells was lower in the animals of the EG compared to the ones in CG for all of the immunomarkers and for the cells found both in epithelium and conjunctive tissue. It was also observed that the animals exposed to ethanol presented less inflammatory cells and their epithelization was slower than in control cases.
Conclusion: Therefore, chronic ethanol ingestion causes a decrease of the DC population during tissue repair in the oral mucosa, which could be related to the delayed healing and low numbers of inflammatory cells.

PS-09-033
Primary oral leiomyosarcoma: A case report with immunohistochemistry findings
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Objective: Leiomyosarcoma is a malignant smooth muscle tumour commonly found in gatro-intestinal tract, retroperitoneal and uterus. It is rarely found in the oral cavity reflecting the paucity of smooth muscle in this region. That, it derived from smooth muscle cells of vascular wall. Our aim is to study the clinico-pathological features of this misleading tumour.
Method: A 28-year-old white male presented a non-ulcerated painless mass of the jaw which was treated by a radical tumour resection with clear margins.
Results: The formalin fixed specimen was processed for histopathological examination which, coupled with immunohistochemistry, and confronted to clinical data concluded to primary jugal leiomyosarcoma. Macroscopically, the surgical specimen constituted of pieces of pale gray, solid tissues measuring 35X30 mm. Section of the biopsy specimen stained with hematoxylin and eosin showed interlacing fascicles of highly atypical spindle shaped cells that had eosinophilic cytoplasm and elongated, blunt-ended hyperchromatic nuclei with frequent mitoses. The tumour cells were strongly immunoreactive for smooth muscle, actin and h-caldesmone. There was no immunoreactivity for S-100.
Conclusion: This study presents a rare case of primary leiomyosarcoma of the jaw which was confirmed by immunohistochemichal staining. This rare diagnosis should be considered by oral health provider ahead of its malignity and the wide range of clinical features.

PS-09-035
Lymphoepithelial carcinoma (LEC) of the sublingual salivary gland: Case report
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Objective: Lymphoepithelial carcinoma (LEC) in salivary glands is very rare, accounting for 0.4 % of the malignant tumours. Generally affecting the parotid gland, LEC has been reported only twice in the sublingual gland. It has significant association with Epstein-Barr virus (EBV). Herein, we report the third case.
Method: A 26-year-old man presented with a palpable mass under the right chin extending to submandibular region for 6 months. Computed tomography scans revealed a 3.5 cm-diameter mass with ill-defined borders in the sublingual region and enlarged lymph nodes in cervical chain. No distant metastasis was detected. The patient underwent an incisional biopsy.
Results: Histologic findings revealed sheets of cohesive tumour nests with dense lymphoid infiltration. Tumour cells had enlarged vesicular nuclei with prominent nucleoli and indistinct cell borders. In situ hybridization for EBV was positive. The patient was diagnosed as LEC. Then right mouth floor resection and bilateral neck dissection were performed. He was discharged without complication and postoperative radiation therapy was planned.
Conclusion: LEC originating from the sublingual salivary gland is uncommon tumour. Therefore, the pathologist should be aware of this entity for proper diagnosis and direct the clinicians towards the treatment modalities based on the small number of previously published cases.

PS-09-038
A rare tumour of the jaw: Clear cell odontogenic carcinoma (CCOC)
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Objective: Clear cell odontogenic carcinoma (CCOC) is a rare intraosseous and locally aggressive malignant tumour of the jaws.
Method: Here we report a case occurred in 46-year-old woman, who admitted to our hospital with a 3 month history of painless swelling in right side of the lower jaw.
Results: The firm, exophytic lesion measuring 3x4 cm was observed involving mandibular right premolar and molar region with exfoliation of 44, 45 and 46, 47. Orthopantomogram revealed the presence of an ill-defined radiolucent destructive lesion in the same region of the mandible. There weren't signs of lymphadenopathy. Diagnosis of CCOC was detected by preoperative incisional biopsy. The patient underwent mandibular resection and reconstruction. Microscopically, sections stained with HE revealed the round to elongated islands and sheets of large clear cells, separated with a thin fibrous hyalinized stroma. Eosinophilic hyaline deposits among the tumour islands were not stained with Congo red. Under higher magnification tumour cells characterized by polygonal, clear cytoplasm with hyperchromatic nuclei and minimal pleomorphism. Mitotic figures were rare. There were no recurrence or metastasis during 36-month follow-up.
Conclusion: CCOC should be on the mental list of the head and neck surgeons, as well as pathologists in differential diagnosis of mandibular masses.

PS-09-039

Prognostic relevance of P53 expression in laryngeal squamous cell carcinoma (LSCC)

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Objective: Evaluate the immunohistochemical expression of p53 in laryngeal squamous cell carcinoma (LSCC) and its correlation with risk factors, tumour location, TNM stage and histological grade.
Method: Our retrospective descriptive study focused on 30 cases of LSCC collected during a period of 6 years from January 2010 to January 2016. A histological examination as well as an immunohistochemical study using the p53 antibody were performed for all the cases.
Results: P53 immunostaining was positive in 15 cases (50 %, $n = 15/30$). The notion of tobacco was found in all these cases (100 %, $n = 15/15$). Alcohol consumption was found in 5 positive cases (33.3 %, $n = 5/15$). The P53 was mostly positive in 11 cases of glottic location (73.33 %, $n = 11/15$). P53 was equally positive with the same percentage in the tumours classified T2N0M0, T3N0M0 and T4N0M0 (each 26.67 %, $n = 4/15$). Regarding the tumour grade, P53 was most frequently positive in 9 cases classified as grade I tumour (60 %, $n = 9/15$). There was only one case of carcinoma in situ. It was positive for P53 (6.67 %, $n = 1/15$).
Conclusion: Our study revealed a correlation between immunoreactivity of p53 and risk factors, tumour location, TNM stage and histological grade. However its prognostic value remains controversial

PS-09-040

Prognostic impact of combined immunoprofiles in patients with oropharyngeal squamous cell carcinoma

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Objective: The objective of this study was to analyze the expression of epidermal growth factor receptor (EGFR), CD44 and p16 in patients with oropharyngeal squamous cell carcinoma (OSCC) and to investigate the significance of expression profiles on radiotherapy treatment outcomes.
Method: This retrospective study included OSCC patients who underwent a definitive radiotherapy in curative intent as a main treatment modality. Expressions of CD44, EGFR, and p16 were immunohistochemically examined in 80 OSCC primary biopsy tumour specimens, analyzed, and correlated with clinicopathological parameters including treatment outcomes.
Results: The positive tumour expression rates of p16, EGFR, and CD44 were 24.8 , 28.8 , and 8 %, respectively. With median follow-up of 39 months, p16 expression was associated with longer survival rates, significant correlation was found between p16 expression and both disease free survival (DFS) and overall survival (OS) rates ($p = 0.004$, and $p = 0.259$). CD44+/p16- displayed the worst, and CD44-/p16+ showed the best survival rates; DFS ($p = 0.0393$); OS ($p = 0.0059$). Combining p16 and EGFR, the worst OS was identified in EGFR+/p16- patients ($p = 0.033$).
Conclusion: Profiles combining CD44, p16, and EGFR expressions detected immunohistochemically seem to be efficient in prediction of prognosis and treatment outcomes in patients with OSCC. Supported by the Czech Health Research Council project 15-31627A.

PS-09-041

Molecular characterisation of odontogenic tumours

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Objective: Odontogenic tumours (OTs) comprise a group of heterogeneous lesions ranging from hamartomatous or non-neoplastic tissue proliferation to benign or malignant neoplasms with metastatic potential. There are various types of this tumour and confusion still exists among clinicians as to its correct classification. A comprehensive molecular prolifing of OTs was performed to identify novel genomic alterations that will led to recognation of molecular classification and influance the new therapeutic approaches.
Method: A total of 50 formalin-fixed, paraffin-embedded OTs samples were sequenced using the Ion Torrent PGM and the 30 gene AmpliSeq Library Kit from 10 ng of extracted DNA. The classification of the OTs was done on hematoxylin-eosin sections according to 2017 World Health Organisation (WHO) classification. The tumours included epithelial (n: 30), mesenchymal (n: 5) and mixed (n: 15) types .
Results: Next generation sequencing analysis displayed that most of the benign OTs(ameloblastoma ,ameloblastic fibroma, Adenomatoid odontogenic tumour,) showed gene mutations in the MAPK signaling pathway with special reference to BRAF and RAS genes (70 %). Multigene alterations were identified mostly in the ameloblastomas when compared to the other odontogenic tumours .
Conclusion: The comprehensive genomic analysis of odontogenic tumours that will be shed new light on fundamental aspects in understanding the molecular pathogenesis of odontogenic neoplasms and may help in the development of new targeted therapies.

PS-09-043

MICA as a biomarker of predisposition to oral squamous cell carcinoma (OSCC)

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Objective: Major histocompatibility complex class I-related chain A (MICA) is a ligand of Natural killer group 2, member D (NKG2D) receptor. Recent studies have shown that MICA is up regulated in tumours from epithelial origin, playing a key role in immunological surveillance.
Method: The aim of our study was to analyze associations of MICA polymorphism with oral squamous cell carcinoma (OSSC). Twenty seven patients with histologically proven OSSC were included in the study. The majority of patients had G2-G3 tumours according to Anneroth's classification. The control group included healthy subjects from Bulgarian population. MICA genotyping was performed by PCR-SSO kit (LABType SSO MICA, OneLambda) and PCR-SBT.
Results: Our results showed statistically significant protective association for MICA*12:01 allele ($Pc < 0.05$, OR-0.07), encoding full length protein. Interestingly this allele had a higher frequency in healthy Bulgarian population compared to other European populations. With the highest frequency in patients with OSSC was observed MICA*08:01 allele, encoding truncated protein. However the difference with the control group was with a borderline significance ($Pc = 0.053$).
Conclusion: Our study confirmed the model that alleles encoding truncated, ectopic and soluble MICA molecules play an important role in OSSC by down regulation of NKG2D on NK and CD8+ T cells leading to aberrant immunological surveillance.

PS-09-044

MicroRNA expression in SMARCB1/INI1-deficient sinonasal carcinoma: A clinicopathological, immunohistochemical and molecular genetic study

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Objective: The aim of the study was to evaluate microRNA expression in SMARCB1/INI1-deficient sinonasal carcinomas.

Method: Polymerase chain reaction was utilized.
Results: A total of 4/56 (7 %) cases of SMARCB1/INI1-deficient carcinomas were detected among 56 sinonasal carcinomas using immunohistochemical screening. The series comprised 3 males and 1 female, aged 27–76 years (median 64 years). All tumours arose in nasal cavity. Three neoplasms were diagnosed in advanced stage pT4. During the follow-up period (range 14–111 months (median 72 months)), three tumours recurred locally, but none of the patients developed regional or distant metastases. Ultimately, two patients died due to the tumour. Microscopically, all tumours were composed of basaloid cells with variable component of rhabdoid cells with eosinophilic cytoplasm. Immunohistochemically, there was diffuse expression of cytokeratins (CK), p16, p40 and p63 in all cases. The detection of NUT was negative. All tumours showed upregulation of both miR-9 and miR-21 and downregulation of miR-145. Regarding miR-99 expression, three tumours featured upregulation and one downregulation. As regards miR-143 expression, two tumours showed upregulation and two downregulation.
Conclusion: In summary, we described four cases of SMARCB1/INI1-deficient sinonasal carcinoma with novel findings on miRNA expression, which might be important for new therapeutic strategies in the future.

PS-09-045
Expression of chemokine receptors, CXCR4 and CXCR7, in salivary gland neoplasms
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Objective: Chemokine receptors have been shown to overexpress in several cancer types. Binding of chemokines to their cognate chemokine receptors on tumour cells can promote tumour growth, angiogenesis and metastasis. The purposes of this study was to examine the expression of chemokine receptors, CXCR4 and CXCR7, in salivary gland neoplasms and its association with pathologic characteristics.
Method: Sixty-two cases of salivary gland neoplasms, including 25 mucoepidermoid carcinomas (MEC), 18 adenoid cystic carcinomas (ACC), 14 pleomorphic adenomas (PA) and 5 polymorphous low-grade adenocarcinoma (PLGA) were investigated for CXCR4 and CXCR7 expression immunohistochemically. The immunoreactivity was categorized in low expression or high expression group, based on whether the positive staining was below or higher than 50 % of neoplastic cells, respectively.
Results: The majority of MECs, ACCs and PLGAs showed high CXCR4 and CXCR7 expression, whereas most PAs showed high CXCR4 but low CXCR7 expression. The levels of CXCR4 and CXCR7 expression were significantly correlated. In MECs, the expression of both chemokine receptors was localized to squamous cells, intermediate cells and glandular epithelial cells, whereas mucous cells and clear cells were negative. In ACCs and PAs, their immunoreactivity was more intense in ductal cells than myoepithelial cells. The increased CXCR4 expression was significantly associated with advanced pathologic grade of MECs.
Conclusion: Overexpression of CXCR4 and CXCR7 is common in 4 salivary gland neoplasms investigated. CXCR4 may play a role in the progression of MECs.

PS-09-046
Clear cell lesions of the head and neck: The spectrum of histological features
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Objective: Head and neck clear cell lesions are rare with a diverse differential including Hyalinising Clear Cell Carcinoma (HCCC), Clear Cell Odontogenic Carcinoma (CCOC), and clear cell variants of mucoepidermoid carcinoma (MEC) and metastatic renal cell carcinoma (RCC). In addition, Sclerosing Odontogenic Carcinoma (SOC) (a recently described lesion) can show clear cell change. EWSR1-ATF1 translocations in HCCC and CCOC can help differentiate these from the other clear cell lesions. Objective- To compare histological and morphological features of clear cell lesions.
Method: Clear cell lesions including CCOC, SOC, HCCC, MEC and RCC were compared using H&E examination, immunohistochemistry and fluorescent in situ hybridisation (FISH).
Results: All showed varying degrees of clear cell change, and stromal sclerosis. HCCC was not as infiltrative as SOC or CCOC, and showed focal mucin globules. SOC had perineural infiltration, and distinct radiological appearances with bone and tooth resorption. CCOC and HCCC showed the EWSR1 rearrangement, but SOC, MEC and RCC were negative.
Conclusion: Clear cell change and stromal hyalinisation can be variable however presence of mucin, inductive change, perineural invasion and radiological correlation can aid diagnosis. Molecular testing is the gold standard and supplements immunohistochemistry in diagnosing HCCC and CCOC, and excluding RCC or MEC.

PS-09-047
The role of Bcl-w in oral squamous cell carcinoma (OSCC)
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Objective: The oral squamous cell carcinoma (OSCC) represents nearly 95 % of all oral malignancies. The Bcl-w is an anti-apoptotic (pro-survival) protein that promotes cell survival by preventing apoptotic proteins from exerting their function. This work aims to study the role of Bcl-w in cell proliferation, tissue invasion and migration in a cell lineage of OSCC.
Method: The OSCC cell lineage SCC25 was treated with ABT-737, which inhibits the activation of Bcl-w. Proliferation analysis of SCC-25 was performed after 48 hrs of incubation with ABT-737 with addition of thiazolyl blue tetrazolium bromide; and the spectrophotometer analysis was performed at a wavelength of 570 nm. For the invasion assay, the nuclei of the cells stained by DAPI invading a later of matrigel were counted 48 hrs after the treatment. The capacity of migration was analyzed making a scratch on the cell plate already at confluence and photographing later to analyze the migration.
Results: A decrease in cell survival, tissue invasion and migration was evident after the Bcl-w blockage.
Conclusion: Our data suggest that Bcl-w pathway may have an important role in cell proliferation and apoptosis as well as in tissue invasion and migration in OSCC.

PS-09-049
Dendritic cells in oral squamous cell carcinoma (OSCC): Is there a difference between young and old patients?
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Objective: There is an increase in the prevalence of oral squamous cell carcinoma (OSCC) in young patients, suggesting the involvement of other factors in the etiology of the disease, including disruption of the immune system. Changes in dendritic cell (DC) maturation and/or activation may contribute to the collapse of antitumour immune response, and therefore lead to disease progression. The present work aims to evaluate the immature (imDCs) and mature (mDCs) dendritic cells immunoprofile in OSCC affecting young and elderly patients.
Method: OSCC samples from 12 patients (aged <40) (G1); 16 patients (aged ≥40 to <60) (G2); and 13 patients (aged ≥ 60) (G3) were analyzed through the imDC (S100, CD1a, CD207) and mDC (CD83 and CD208) immunomarkers. The occurrence and localisation of immunostained DCs were analyzed in intratumoural (intranestal and/or extranestal) and extratumoural areas and submitted to statistical analysis.

Results: imDCs and mDCs were more frequent in intranestal and extranestal localisation, respectively. G1 showed a considerable lesser number of both imDCs and mDCs when compared to G2 or G3.
Conclusion: The lower amount of both imDCs and mDCs in OSCC affecting young patients may suggest an impairment of an effective antitumour immune response in younger patients.

PS-09-050
Twist and snail expression in the lining epithelium and connective tissue wall of developmental odontogenic cysts
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Objective: Expression of E-cadherin repressors has been investigated recently in a few odontogenic cysts. The aim of this study was to evaluate expression of Twist and Snail in the lining epithelium and connective tissue wall of developmental odontogenic cysts.
Method: Immunohistochemistry was performed using antibodies against Twist and Snail in 20 cases each of dentigerous cyst (DC), odontogenic keratocyst (OKC), recurrent OKC (ROKC), orthokeratinized odontogenic cyst (OOC), and 13 cases of glandular odontogenic cyst (GOC).
Results: All of the cysts but 1 ROKC showed negative Twist expression in the lining epithelium. In connective tissue walls, ROKC and GOC showed stronger Twist expression compared to the other cysts ($P = 0.003$). Higher Snail expression was found in the lining epithelium ($P = 0.003$) and connective tissue wall ($P < 0.001$) in OKC, OOC, and GOC compared to DC. A weak positive correlation was observed between epithelial and connective tissue expression of Snail ($r = 0.225$, $P = 0.030$).
Conclusion: Despite its absence in the lining epithelium, Twist may contribute to aggressive behavior and recurrence of developmental odontogenic cysts in the connective tissue wall. Snail may be associated with the pathogenesis of OKC, OOC, and GOC via paracrine interactions between epithelial and connective tissue components.

PS-09-051
Unusual pleomorphic adenomas: A pitfall in salivary gland pathology
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Objective: Pleomorphic adenoma (PA) is considered a benign epithelial-derived tumour. The aim of this study is to discuss and illustrate some of the unusual salivary PA that the practicing pathologist find difficult to diagnose.
Method: The cases were selected over a period of 10 years from the Pathology Department, City Hospital of Timisoara. We identified 279 cases of salivary gland tumours.
Results: We found that 126 cases were PA, 76 cases were female and 50 cases were male, with ages between 11 and 83 years old. One hundred eight cases of PA showed tipically features and were described as round to ovoid tumours with well-defined borders composed of both epithelial and mesenchimal-like tissue. In 18 cases PA had distinctive histopathological features. We found 1 case of lipomatous PA, 1 case with prominent osseous differentiation, 2 cases of atypical PA, 2 cases with squamous differentiation, 1 case with oncocytic cells, 1 case of cystic PA, 6 multinodular PA (with 2 recurrent PA), 3 with intracapsular invasion and one case of giant PA (with size 12/14/7 cm).
Conclusion: PA can sometimes present with gross and histopathological aspects containing unusual elements which could be unrecognized and risk misdiagnosis.

PS-09-052
Ossifying fibromas of the head & neck: A clinical, radiological and histopathological review
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Objective: Ossifying fibromas (OF) show a range of clinicopathological features, but comprise three types: cemento-ossifying fibroma (COF), which is an odontogenic neoplasm, and two juvenile types—trabecular (TOF) and psammomatoid (POF). Our aim was to determine if histology can clearly distinguish odontogenic (COF) from non-odontogenic (NO) (TOF, POF) lesions.
Method: OF were retrieved and classified COF or NO according to site and relationship to teeth. Histological assessment ($n = 69$) included the border of the lesion, secondary changes, and pattern of calcification, defined as trabecular, psammomatoid or mixed.
Results: Overall 67 % of OFs were painless and >90 % were well demarcated and unilocular. Histologically 70 % were circumscribed with a highly cellular stroma (84 %) and low vascularity (81 %). 55/69 lesions (80 %) were COF, 80 % (44) of which were in the mandible. Only 4/14 (28 %) NO arose in the mandible, with 64 % in the maxilla or antrum. Most COF were psammomatoid (56 %). NO lesions were TOF (7/14:50 %), POF (36 %) or mixed (14 %). Calcification pattern did not correlate with origin. Multinucleated giant cells (32 %) and aneurysmal bone cysts (3 %) were also noted.
Conclusion: A psammomatoid pattern is common (52 % of OF) and 83 % of odontogenic lesions are found in the mandible. Histology alone cannot distinguish between types.

PS-09-053
Mucosal melanoma of head and neck: A report of 13 cases
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Objective: The purpose of this study was to report 13 cases of of mucosal melanoma of the head and neck (MMHN) and to discuss pathological features.
Method: We report here 13 MMHN treated at the Department of Head and Neck Surgery in Salah Azaiez Institute of Tunis since 1980 to 1999. Clinical data were obtained from the patient's charts. Analysis of pathological features, type of therapy and follow-up was retrospectively reviewed.
Results: The mean age was 71 years (range 38 to 100 years), there were 7 men and 6 women. The site of the tumour was the lateral wall of the nasal cavity (six cases), nasal septum (two cases), maxillary cavity (two case), ethmoidal diffused to orbital cavity (one case) and internal mucosal jaw (two cases). Surgery was performed in 12 patients; adjuvant radiation therapy was used in nine patients after local recurrence and chemotherapy in 11 patients. Nine of 13 patients (69, 2 %) had a recurrence after previous treatment (surgery). The actuarial disease-free survival for is 33.7 % (4 of 13). Histopathologial features demonstrate a non-pigmented melanoma in 7 cases. HMB45 and PS100 were positives in 100 % of cases.Molecular study was not performed.
Conclusion: MMHN is an aggressive tumour with a bad prognosis. This neoplasm requires confirmatory immunohistochemical stains. Recent molecular findings demonstrate a different biology from cutaneous one and offer new hope for the development of more effective systemic therapy.Indeed, proto-oncogene KIT aberrations in a subset of mucosal melanomas may represent a potential diagnostic value and serve as a therapeutic target for tyrosine kinase inhibitors in an adjuvant setting for patients with advanced MMHN.

PS-09-054

Primary mucosal malignant melanoma of the larynx: A case report

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Objective: Background: Primary laryngeal mucosal malignant melanomas are uncommon tumours that morphologically are readily confused with more common types of laryngeal cancer.
Method: This report describes a case of primary malignant melanoma arising in the larynx and diagnosed by histologic examination of an biopsy specimen.
Results: Case The patient was a 55-year-old man with a history of smoking and hoarseness. It was seen showed a dark gray to red colour alteration areas at anterior comissure and cord vocale in the laryngoscopy.The patient was performed biopsy.There was no clinical evidence of other primary malignant melanocytic lesions. Microscopically, the tumour consisted of polygonal and epithelioid cells admixed with more elongated, spindle-shaped cells. The majority of the cells demonstrated dark brown cytoplasmic and nuclear melanin. Marked pleomorphism and abnormal mitoses were also identified. Immunohistochemical studies were positive for S100, Melan-A,HMB-45 and vimentin, while cytokeratin and iron stains were negative. Based on the clinical and histologic findings, a diagnosis of primary malignant melanoma of the larynx was established. Fontana stains confirmed the presence of melanin . The patient was lost to follow-up.
Conclusion: Primary laryngeal mucosal melanomas are very rare but aggressive tumours. The diagnosis of melanoma is based on histopathological examination and immunohistochemical stains, but in order to diagnose a primary laryngeal melanoma any other primary lesion (cutaneous or mucosal) it has to be excluded. Key Words:Larinx, malign melanom,mucosal,primary

PS-09-055

Follicular dendritic cell tumour of tonsils: Report of 2 cases

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Objective: Follicular dendritic cell sarcomas (FDCS) are uncommon; they can primarily arise in lymph nodes or at extranodal sites. We describe here two cases of tonsillar FDCS.
Method: Clinical details, pathologic features, immunohistochemical profile, treatment approach and outcomes of two cases of FDCS.
Results: Both patients are men, 1st 56 and 2nd 33 years old, presented with unilaterally enlarged tonsils. Tumours were surgically removed. The 2nd patient underwent adjuvant radiotherapy (50Gr). Microscopically in each case sheets, whorls, and storiform arrays of spindly and syncytial-appearing cells with oval nuclei, fine chromatin, distinct nucleoli, and occasional nuclear pseudo-inclusions characterized tumour. Multinucleated cells were present in the 1st case. In this case, irregular pseudovascular spaces were seen rising concern for vascular neoplasm. Immunohistochemically, each tumour was typified by expression of CD21, CD23, CD68, Vimentin, Fascin. Ki67 – 10 %. Whereas cells were completely negative with antibody to panCK, EMA, LCA, CD1a, CD2, CD3, CD20, CD30, CD34, CD43, CD79a, cyclinD1, Bcl-2, MPO, ALK, EBV, LMP, S100, EGFR, SMA, Desmin, HMB 45. Both patients are free of disease for 8 (1st) and 6 (2nd) months.
Conclusion: A high index of suspicion allows diagnosing FDCS. Surgery is the mainstay of treatment; the advantage of radiotherapy is unclear yet.

PS-09-056

Multifocal extranodal Rosai-Dorfman disease affecting the cavernous sinuses and the skin - a case report

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Objective: Intracranial extra-nodal Rosai-Dorfman disease (ERDD) is rare. To our knowledge 6 cases of cavernous sinus disease have been reported. We report a case of ERDD affecting the cavernous sinuses and the skin, and highlight the difficulty of diagnosis.
Method: A 56-year-old diabetic man presented with a week history of double vision of 1 week duration and pain behind the left eye. Examination revealed a left sixth cranial nerve CNVI palsy and ptosis. CT head showed an abnormal enhancing lesion within the left cavernous sinus extending to the orbital apex. PET CT showed avid uptake of this lesion and focal uptake in the a skin lesion on the back. Skin biopsy was suggestive of fungal infection and the differential diagnoses of skull base lesion included metastatic melanoma, lymphoma, sarcoidosis and fungal infection.
Results: Biopsy of skull base lesion showed numerous characteristic histiocytes with emperipolesis in a background of lymphocytes and plasma cells. Immunocytochemistry revealed the histiocytes stained positive for CD68 and, S-100, but negative for CD1a. Diagnosis was ERDD, and subsequently, the back lesion was diagnosed. The patient underwent chemoradiotherapy, commenced steroids and methotrexate. Two years after diagnosis the patient continues steroids to control symptoms.
Conclusion: ERDD is rare. An atypical presentation and radiological mimics poses a diagnostic challenge. A wide differential diagnosis includes neoplasia, infection and inflammation. Therefore, Histopathology is essential for definitive diagnosis and appropriate treatment.

PS-09-057

Laryngeal cryptococcal infection in immunocompetent patient mimicking a malignant tumour

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Objective: Cryptococcal laryngitis has been seen in patients with AIDS either with previous or concurrent pneumonia or as isolated laryngeal lesions. It may also occur in immunocompetent hosts with or without concomitant pulmonary disease. Clinically it has an exudative or a wart-like appearance but may rarely present as a smooth-surfaced mass.
Method: A 70 years old immunocompetent man was submitted to our hospital with hoarseness and respiratory distress. Imaging studies and laryngoscopy was suspicious for malignancy.
Results: A vocal cords biopsy was performed and tissue fragments were sent to our lab, measuring 0,6x0,4x0,1 cm. Microscopic examination revealed acute intraepithelial inflammation of laryngeal mucosa and heavy chronic inflammatory infiltrate in the lamina propria comprising mainly of plasmacytes and among them numerous capsule yeasts.
Conclusion: Cryptococcal laryngeal infection is uncommon, especially in immunocompetent patients, with so far only 21 documented cases. Clinical presentation, laryngoscopic findings and imaging results may mimic a neoplasm. Histopathological examination can demonstrate the causative organism so that proper treatment can be achieved.

PS-09-058

Quercetin induced oral tissue & minor salivary glands remodeling under experimental type 2 diabetes mellitus

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Objective: Diabetes mellitus is associated with a greater probability of developing oral mucosal lesions. The aim of the study was to evaluate the effect of bioflavonoid quercetin upon the rats' mucous membrane of a cheek, tongue and on minor salivary glands under alloxan-induced hyperglycemia conditions.
Method: Diabetes was induced in 42 Wistar rats with the intramuscular injection of the protamine sulfate. Long-term administration of protamine sulfate caused persistent hyperglycemia, reduced glucose tolerance and high insulin resistance. Animals were divided into experimental (1st) and group of comparison (2nd). 1st group of animals was treated with the bioflavonoid quercetin supplementation. Oral tissues and salivary glands samples were examined morphologically, then with the help of computer morphometry.
Results: Experimental metabolic abnormalities resulted in pathological changes of cheek and tongue mucosa, minor salivary glands injuries. The quercetin application has stimulated the angiogenesis in oral tissues. Blood circulation disorders were fewer in 1st group of animals. Volume fraction of the edematous oral mucous membrane decreased by the end of the 2nd week of the experiment. Zones of structural injuries were replaced with areas of tissue repair and enhanced vascularity.
Conclusion: Antioxidant characteristics of the quercetin stimulated the adaptive oral and minor salivary glands tissue remodeling, contributed improved repair processes.

PS-09-059

Metastatic squamous cell carcinoma (SCC) of the parotid: A case of an occult primary

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Objective: Metastatic carcinoma involving the parotid lymph nodes is an uncommon and potentially overlooked possibility in the patient presenting with a parotid mass. In the vast majority of cases, these lesions originate from cutaneous malignancies that either metastasize by regional lymphatic spread or invade by contiguous spread. We present a case of SCC metastatic to an intraparotid lymph node which masqueraded as a primary lesion.
Method: A 77-year-old man was presented to our hospital with a 4-month history of a painless left preauricular mass. Physical examination showed an approximately 2 cm mass in the body of the left parotid gland. There was no fixation to the skin and no change in the overlying skin texture. He underwent a left parotidectomy.
Results: Histologic examination revealed an intraparotid lymph node occupied by a metastatic squamous cell carcinoma of moderate to low differentiation. The primary site of origin was not apparent. Further investigation and correlation with clinicopathologic findings was sought.
Conclusion: Metastatic squamous cell carcinoma (SCC) involving an intraparotid lymph node, although uncommon, remains of practical consideration in the differential diagnosis of a parotid mass. This is of particular importance when the primary lesion is not readily identifiable, or has been inadequately managed in the past.

PS-09-060

Human papillomavirus (HPV)-related carcinoma with adenoid cystic-like features: A case report and review of the literature

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Objective: HPV related carcinoma with adenoid cystic like features is recently described sinonasal carcinoma resembling adenoid cystic carcinoma but the main features that lead to this diagnosis are the presence of surface epithelial dysplasia and HPV positivity.
Method: A 85-year-old male patient with a history of excised nasal mass in 2006 and then again at 2011, reported as basal cell carcinoma and sinonasal adenocarcinoma respectively, was admitted for recurrent lesion detected at the same location in the follow-up at 2016. Punch biopsy revealed tumoural infiltration positive with cytokeratin AE1-AE3, p63, p40, cytokeratin 5/6, p16 and negative with cytokeratin 7, cytokeratin 20, CEA-mono, CD117, smooth muscle actin, S100, synaptophysin, CDX2. HPV type 16 positivity was detected with quantitative polymerase chain reaction.
Results: .
Conclusion: This patient has been followed with misdiagnosis for about 10 years due to the new definition of this entity. This process gives an idea of the clinical course of this rare tumour. Because it is a new entity and the differential diagnosis is difficult, it is aimed to be discussed with all the literature cases (only 15 cases have been reported so far) and to be reminded of the case.

PS-09-061

Mikulicz's syndrome associated with leukemia: A case report

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Objective: Mikulicz's syndrome is extremely rare chronic swelling of the lacrimal and major salivary glands usually associated with decreased or lack of lacrimation, xerostomia and accompanied by lymphocytic infiltration. It is associated with other entities like tuberculosis, lupus erythematosus, lymphoma, leukemia, etc.
Method: A case of 70 years old man with painless, dense swelling of left parotid gland and medical history of leukemia is presented. Decreased secretory activity of the parotid gland is observed. The patient is referred for laboratory blood test and ultrasound assessment of the parotid and thyroid glands.
Results: Mikulicz's syndrome associated with acute myelogenous leukemia was identified. The secretory activity is compensated by the remaining minor and major salivary glands and there are no complaints of significant xerostomia. Laboratory blood test reveals leukocytosis (118 g/L). Results from ultrasound assessment of the glands demonstrate no obvious changes. The progress of the disease seems to be associated with the main disease severity and appears to be a poor prognostic sign - the patient died after a week.
Conclusion: Based on the clinical findings the definitive diagnosis was Mikulicz's syndrome associated with leukemia was established. The swelling is expected to disappear spontaneously or after treatment with corticosteroids.

PS-09-064

Epithelioid sarcoma of the tongue

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Objective: Epithelioid sarcoma involving the tongue is extremely rare. We report a 50-year-old male who was operated due to a nonulcerated lesion in the left border of the tongue and metastatic dissemination to the

cervical lymph node. The histopathological examination revealed epithelioid cells with abundant eosinophilic cytoplasm and atypical nuclei. Immunohistochemically, the tumour cells stained for vimentin, CK8 and epithelial membrane antigen and negative for CK5/6, p63, c-kit.
Method: A 50-year-old male presented with a tumour in the left border of the tongue and a cervical lymph node metastasis. The patient underwent resection of the tumour, lymph node dissection, and postoperative radiotherapy was performed after the operation, despite tumour free margins.
Results: The tumour was 2 cm in the greatest dimension, and the cut surface was gray-pink with zones of hemorrhage without necrosis. Histologically, tumour cells were epithelioid, with abundant eosinophilic cytoplasm and atypical nuclei. Immunohistochemically, the tumour cells stained for vimentin, CK8 and epithelial membrane antigen , and negative for CK5/6, p63, c-kit.
Conclusion: Epithelioid sarcoma with localisation in the extremities is well known in pathology practice. This case is valuable due to its rarity.

PS-09-065
Carcinosarcoma of the tongue: A unique diagnosis
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Objective: Carcinosarcoma was initially described by Virchow in 1864. Since then, the largest landmark study on this entity has been that of Batsakis et al, who described three different categories of this tumour, namely: pleomorphic (spindle cell) carcinoma, carcinoma with pseudosarcomatous stroma and carcinosarcoma. The latter is extremely rare in the oral cavity.
Method: An 85-year-old male was referred to the ENT Department, complaining of a rapidly growing tongue mass. Clinical examination revealed a 40 × 35 × 20 mm polypoid mass at the left lateral border of the tongue.
Results: Histopathologic examination of the resected tumour revealed a biphasic neoplasm composed of both malignant epithelial and mesenchymal components. In the former, the neoplastic cells displayed a solid, trabecular or cribriform pattern and were positive for CK7. The mesenchymal element consisted of epithelioid and spindle cells with pleomorphic nuclei and brisk mitotic activity which were positive for vimentin and caldesmon but negative for desmin and S-100 protein. Consequently, a diagnosis of carcinosarcoma was set.
Conclusion: Surgery followed by adjuvant radiotherapy is the treatment modality of choice for patients with carcinosarcoma of upper aerodigestive tract. The role of re-excision in patients with positive surgical resection margins is paramount. Rarity precludes treatment modalities comparison studies.

PS-09-066
A complicated case of adenoid cystic carcinoma
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Objective: To describe an unusual case of adenoid cystic carcinoma (ACC).
Method: A 54 year-old woman presented with a mass of the palate. MRI showed a 40 mm tumour, invading bone and the sinonasal cavities. ACC was diagnosed on biopsy. Large surgery was performed, followed by radiotherapy. After several recurrences, this tumour was treated with Herceptin.
Results: Histologically, this tumour had a central portion of ACC, in the palate and the maxillary bone, mostly formed of solid nests with some glandular structures ; and a peripheral portion of high-grade poor differentiated carcinoma, localized in the sinonasal mucosa, with secondary invasion of its epithelium. In both components, C-Kit and p63 were positive, but the myoepithelial markers were negative. In the peripheral high-grade component, ki67 was higher and p16 was overexpressed, without evidence of HPV-HR by CISH, rouling out the possibiity of a «HPV-related carcinoma with adenoid cystic-like features ». Her2/neu status was 2+ in the central portion and 3+ in the peripheral high-grade component. FISH confirmed the overexpression of HER2. The search for the MYB-NFIB fusion is ongoing.
Conclusion: This case illustrates the diagnostic problem of ACC with dedifferentiated or high-grade component, and the potential theranostic interest of testing HER2 in some reccurent ACC.

PS-09-067
MMP-9 and TIMP-1 expression in tooth development
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Objective: The precise role of MMPs in tooth development is still unknown. Our study focused on the evaluation of MMP-9 and TIMP-1 as evidence of matrix remodeling potential in tooth development.
Method: The material comprised teeth germs from 15 fetuses obtained from medical or spontaneous abortions, with gestation age between 10 and 24 weeks. The cephalic extremities and/or mandibles fragments carefully removed and dissected were routinely processed for histopathology and immunohistochemistry. MMP-9 and TIMP-1 expressions were quantified as scores obtained from the sum of positive cells percentage and staining intensity.
Results: Our results showed a simultaneous expression of MMP-9 and TIMP-1 in odontogenesis, without differences between the deciduous tooth germs, corresponding to medial and lateral incisors, canine, and molars. Cap stage was characterized by balanced MMP-9 and TIMP-1, strong in the enamel organ epithelium and weak in dental papilla cells. We noted MMP-9 predominant expression - especially in the odontoblasts, as compared to TIMP-1, in the bell stage. The qualitative assessment was sustained by the score values.
Conclusion: The expression of MMP-9 and TIMP-1 in ameloblasts and odontoblasts represent important marker for the differentiation of these cells which results in organic matrix synthesis and mineralization of enamel and dentin.

PS-09-068
Small lymphocytic lymphoma as a random finding in lymph nodes with metastasis from an undifferentiated carcinoma of the submandibular salivary gland
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Objective: A 75-year-old female patient presented with an oral cutaneous fistula, originating from a tumour of the submandibular salivary gland. An unexpected finding in the cervical lymph nodes was revealed.
Method: Following extended excision of the tumour, as well as cervical lymphadenectomy, the material was examined with hematoxylin-eosin and immunohistochemical stains.
Results: Microscopic examination revealed the presence of an undifferentiated carcinoma of the submandibular salivary gland, infiltrating the overlying skin, and metastasized to two of the examined lymph nodes. The neoplastic cells were positive for AE1/AE3, p63 and CD56. Moreover, all of the lymph nodes demonstrated effacement of architecture, due to infiltration by small lymphocytic lymphoma, consisting of malignant small lymphocytes, arranged in a diffuse growth pattern. Their immunophenotype included positive staining for CD20, CD79a, CD5 and CD23 and negative staining for CD10 and cyclin D1.

Conclusion: The undifferentiated carcinoma of the salivary gland belongs to poorly differentiated carcinomas and is usually located in the parotid gland. We report the case of an undifferentiated carcinoma of the submandibular salivary gland, simultaneously with the random finding of small lymphocytic lymphoma in the cervical lymph nodes. To our knowledge, there is no documentation of similar cases in the literature.

PS-09-069

Salivary gland tumours - a study of 30 Romanian cases

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Objective: Although salivary glands neoplasms are rare (~6 % of head and neck tumours), they include a large variety of both benign and malignant types, more frequent at women with a high frequency in elderly. Majority arise in the parotid, the rest in the submandibular, sublingual and minor salivary glands.
Method: We present a study of salivary glands tumours during a period of 3 years at the National Institute "Victor Babe", using histological and immunohistological metods. IBM SPSS Statistics version 20.0 (SPSS Inc., Chicago,Illinois,USA) was used for data analysis.
Results: We studied 30 cases, 18 males and 12 females, aged between 22 and 80. The most frequent affected regions were the parotid (14), minor salivary glands (13), lips (2) and palate (1); 24 tumours were primitive and the rest metastasis. Primitive malignant tumours were salivary duct carcinoma (5), mucoepidermoid carcinoma (3), adenoid cystic carcinoma (2), acinic cell carcinoma (2), carcinoma ex pleomorphic adenoma (3) and basal cell adenocarcinoma (1). Among benign tumours, the most frequent was pleomorphic adenoma (3). The six cases of metastases were a Merkel cell neuroendocrine carcinoma, hepatocarcinoma, adenocarcinoma with a digestive origin, scuamous cell carcinoma, small cell carcinoma and spindle cell carcinoma. Statistical analysis revealed an indirect correlation between age and tumour location at women.
Conclusion: In our study, parotid and minor salivary gland locations were the most frequent; among primitive tumours, malignancy represent a high proportion (66,6 %) and the most frequent was salivary duct carcinoma; we also observed that 20 % of cases were metastasis.

PS-09-070

Granular cell tumour of the tongue: A case report

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Objective: Granular cell tumour is a relative uncommon benign neoplasm of unknown etiology which characterized by accumulation of plump cells with abundant granular cytoplasm.About 45–65 % of all cases occur in the head and neck region and of these 70 % located in the oral cavity. We report a case of 52-year old female with agranular cell tumour of the tongue.
Method: The patient visited the hospital complaining of a swelling on the dorsum of the tongue. On intraoral examination revealed a firm, well circumscribed,non-tender lesion, measuring 0,8x0,6 cm on the dorsal of the tongue. Surgical excision of the lesion was done and the histological examination showed a well defined, not encapsulated nodule in a focal area of submucosal connective tissue. There were pseudoepitheliomatous hyperplasia of the stratified squamous epithelium beneath which there were large polyhedral cells with eosinophilic granular cytoplasm and pyknotic nuclei, positive to S-100.
Results: The histological examination confirmed the definite diagnosis of granular cell tumour of the tongue.
Conclusion: Recognition of this uncommon neoplasm might help the surgeon for the correctly diagnosis and surgical treatment of these tumours.

PS-09-071

Cavernous haemangioma of the tongue: A rare case report

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Objective: Haemangiomais a benign vasoformative neoplasm that is histologically classified into capillary and cavernous form. It is most commonly seen in the head and neck region but their occurrence on the tongue is extremely rare. We report a case of 34-year old female with a cavernous haemangioma of the tongue.
Method: The patient visited the hospital for a localized slow growing lesion on the posterior third of the tongue. On intraoral examination, there was a sessile, red, pulsatile with well defined margins lesion measuring 0.6x0,5 cm on the posterior third of the tongue. Excision of the lesion was done with no postoperative complications. The histological examination showed a well defined, not encapsulated nodule in a focal area of submucosal connective tissue with multiple dilated thin walled vascular channels filled with blood and lined by endothelial cells. The vascular channels areseparated by scanty connective tissue stroma.
Results: The histological examination confirmed the definite diagnosis of cavernous haemangioma.
Conclusion: Early detection is crucial in determining the clinical behavior of the tumour and potential complications. The treatment modality should be planned according to the diagnosis.

PS-09-072

Salivary gland oncocytic carcinoma: A very rare entity

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Objective: Salivary oncocytic carcinomas account for 0.5 % of all epithelial salivary gland malignancies and 0.18 % of all epithelial salivary gland tumours. We present a case report of oncocytic carcinoma (OC) of the parotid gland to further characterise its gross and microscopic appearance.
Method: A 64-year-old man presented to the Oro-Maxillo-facial Surgery Department, City Hospital of Timisoara, with a right parotid painless mass. A resection of the mass with tumour-free margins and removal of the ipsilateral cervical lymph nodes was performed.
Results: Macroscopicaly the tumour was a well-circumscribed 5.5/3/4.5 cm soft mass with solid and cystic areas and yellow to tan-brown color cut surface. Microscopic examination revealed a solid OC with cystic areas and large, round-oval or polyhedral oncocytic cells and a fibrous stroma. The tumour cells had eosinophilic, abundant, finely granular cytoplasm and round-to-oval, centrally or eccentraly located pleomorphic nuclei with prominent nucleoli and rare mitotic figures. Necrosis was present in some solid and cystic areas of the tumour. There were no lymph node metastasis.
Conclusion: Because OC is a rare salivary malignancy with unclear prognosis and treatment options patients should be carefully follow-up for a long period of time.

PS-09-073

Solar elastosis in actinic cheilitis: A histomorphometric and histochemical study

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Objective: Actinic cheilitis (AC) is a potentially malignant disorder characterized by epithelial and connective tissue alterations caused by chronic

exposure to ultraviolet (UV) radiation. Solar elastosis (SO) represents the photodamage caused by UV radiation in lip lamina propria. This study aimed to assess the extension and density of SO and its relation with different degrees of epithelial dysplasia in AC.
Method: SO was evaluated through histochemical reactions with Picrossirius Red and Weigert's risorcin-fuchsin. Epithelial dysplasia was evaluated according to WHO grading system. Elastosis extension was measured and scored 1–4 according to elastic fibres density. Student's t test and logistical regression were performed and statistical significance was set at $P < 0.05$.
Results: Elastotic material was positively stained with risorcin-fuchsin. AC cases with moderate and severe epithelial dysplasia had an increased extension of SO and higher scores of density. SO was closer to the epithelium in cases with severe dysplasia ($P < 0.05$).
Conclusion: We observed that SO is composed mainly by degenerated elastic fibres and that it is significantly related to epithelial dysplasia grading in cases of AC. Therefore, the extension and density of photodamage in connective tissue reflect the epithelial alterations that occur in AC.

PS-09-074
Oncocytic lipoadenoma of the submandibular gland: A peculiar case of a rare entity
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Objective: Oncocytic lipoadenoma is an extremely rare salivary gland tumour with less than 30 cases reported in the literature to date. These tumours primarily occur in elderly males, usually in the parotid gland, followed by the minor salivary glands than the submandibular gland.
Method: We report a case of oncocytic lipoadenoma occurring in the submandibular gland of a 50 year old female. A comprehensive literature review was carried out and the findings tabulated and compared with our case.
Results: The patient presented with a submandibular mass seen on neck ultrasound. FNA of this mass was non-diagnostic with only a few clusters of benign acinar cells being present. A formal excision was done, and macroscopic examination of the specimen showed a well circumscribed tumour with a homogenous yellow cut surface. On microscopy the tumour was unencapsulated, and was predominantly composed of sheets of mature adipocytes in which aggregates of oncocytes as well as occasional ducts and groups of acinar cells were seen.
Conclusion: Oncocytic lipoadenoma is a rare benign tumour most commonly occurring in the parotid gland, with only a handful of cases occurring in the submandibular gland reported in the literature. The differential diagnosis includes sialolipoma and salivary gland oncocytic tumours.

PS-09-075
A large nasal mass revealing a primitive thyroid carcinoma
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Objective: Metastasis of thyroid carcinoma usually occurs in lymph nodes or bones, however other sites such naso-sinusian mucosa are extremely rare. To our knowledge only three cases of nasosinian metastasis of a thyroid carcinoma have been described in the literature. We report a new Tunisian case.
Method: A 43-year-old patient consulting for paresthesia of the right hemi-face associated with nasal obstruction. Physical examination revealed a mass of the nasal fossa with a large thyroid nodule. In imaging, it was a large mass of the right spheno palatine fossa that extends from the tonsillar sella to the right maxillary gland. A biopsy of the nasal lesion was performed.
Results: The biopsy revealed a poorly differentiated carcinoma (PDC), arranged in nests and cordons. At immunochemistry, tumour cells expressed CK and thyroglobulin.
Conclusion: PDC of the thyroid is an aggressive malignant tumour. In addition to local invasion, the majority of patients present at the time of diagnosis distant metastases. A revealing nasal location is exceptional. Since it is a poorly differentiated tumour, it poses a major diagnostic problem. The primordial immunochemical study by a thyroid marker is necessary.

PS-09-076
Bone tumours of the face: Anatomo-clinical study of 26 cases
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Objective: Bone tumours of the face (BTF) gather very varied histological entities. Radiological examination would often suggest the diagnosis and histological examination is mandatory to confirm the diagnosis. The aim of our work is to study the epidemiological and clinical profile of BTF as well as their pathological characteristics and their evolution.
Method: Our retrospective study included 26 BTFs, collected between 2000 and 2014.
Results: The mean age was 36,9 years with a sex ratio of 2,2. Clinical signs were dominated by swelling. Our series included 21 benign tumours (81 %) and 5 malignant tumours (19 %). These were 12 odontogenic tumours: 8 keratocysts, 1 dentigerous cyst, 1 ameloblastoma, 1 complex odontoma and 1 odontogenic fibroma. The study showed 14 non-odontogenic tumours: 5 chondrosarcomas, 4 osteomas, 1 fibrous dysplasia, 1 osteoid osteoma, 1 ossifying fibroma, 1 osteochondroma, and histiocytosis X. The treatment was surgical in all cases. Complete tumour excision was performed in 18 patients. Radical surgery was performed in 8 patients with osteomas and chondrosarcomas. A patient with grade III chondrosarcoma had radiotherapy and two patients with grade II chondrosarcoma received chemotherapy. A tumour recurrence occurred in 9 (35 %) patients with osteomas, chondrosarcoma, keratocyst, fibrous dysplasia, and ameloblastoma.
Conclusion: Because of their scarcity and diversity, BTFs present a diagnostic dilemma. The pathologist must rely on clinical data and morphological findings to establish the adequate diagnosis.

Monday, 4 September 2017, 09:30–10:30, Hall 3
PS-10 Molecular Pathology

PS-10-001
MicroRNA signature associated with KRAS-mutated colorectal cancer
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Objective: KRAS gene mutations play an important role in the activation of RAS-RAF-MEK-ERK signaling pathway in colorectal cancer (CRC) progresion. Recent studies have shown that microRNAs (miRNAs) signature is associated with specific tumour subtypes. This study aimed to determine the miRNA signature in KRAS-mutated CRC.
Method: We studied fresh-frozen fixed in RNAlater tumour fragments from 18 patients with CRC. To identify miRNA signature we used Human Cancer Pathway Finder miRNA PCR Array, Qiagen, USA, comparing 10 mutant with 8 wild-type KRAS tumours (codons 12, 13, 59, 61, 117 and 146). Analysis of the results was performed using Free miRNA PCR Array Data Analysis, Qiagen, USA.

Results: The presence of the KRAS mutation was associated with 14 downregulated miRNAs: miR-132, let-7d, miR-138, let-7i, miR-10a, miR-15b, miR-193b, miR-181d, miR-100, miR-98, let-7f, miR-181c, miR-128 and miR-155 (p = 0,004÷0,043)
Conclusion: We identified a specific miRNA signature associated with KRAS mutation in CRC. Larger series of patients are necessary for application of these miRNAs as predictive/prognostic markers and as promising candidate in the better stratification of CRC patients. This work was supported by PN 16.22.01.02 and POSCCE 173/2010.

PS-10-002
Frequency of RAS mutation among patients with metastatic colorectal cancer in Hungary on the base of the results of the National Institute of Oncology
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Objective: A confirmed wild-type RAS tumour status is commonly required for prescribing anti-EGFR treatment for metastatic colorectal cancer. In Hungary in the molecular pathology laboratory of the National Institute of Oncology we routinely analyze metastatic colorectal cancers' RAS status since 2010. Our aim was to analyze the RAS mutation frequency in our material.
Method: 655 metastatic colorectal patients' RAS mutation data were collected from 2015. Mutation analyzes of KRAS and NRAS exon 2,3,4 was done by COBAS 4800 KRAS kit and in house PCR based method combined with Sanger sequencing validated in ESP KRAS EQA.
Results: RAS mutation frequency from 655 tumour samples tested for RAS mutation status was 48 %. 88,5 % of RAS mutation was KRAS exon 2, 1,4 % KRAS exon 3, 6 % KRAS exon 4 and 2 % NRAS exon 2 and 3 mutation respectively. We did not detect NRAS exon 4 mutations in any of the cases. RAS mutant tumours were predominant in left sided colon and rectum. RAS mutation was more frequent in men. Mean turnaround time of the reports was 8 days.
Conclusion: Our results of RAS mutation analyzes are in accordance with worldwide data.

PS-10-003
Role of single nucleotide variations in the IL-17A and IL-17 F genes in colorectal cancer susceptibility and progression
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Objective: Recent evidence have elucidated the role of Interleukin-17 (IL-17) in colorectal cancer (CRC) development. IL-17 could stimulate angiogenesis in CRC cells and thus promote tumour growth and metastasis. Accordingly, we aimed to investigate the association of IL-17A G197A (rs2275913) and IL-17 F T7488G (rs763780) single nucleotide polymorphisms (SNPs) with the susceptibility to CRC.
Method: Both SNPs were detected by RFLP-PCR in a group from the Bulgarian population. Th17-positive lymphocytes were counted immunohistochemically in all CRC patients.
Results: A statistically significant case-control difference in genotype frequency for the IL-17A G197A emerged (p = 0.028, $\chi 2$ = 7.13). It appeared that the carriers of the heterozygous (AG) genotype have 2.81-fold lower risk for CRC compared to the homozygous genotypes (AA and GG) (OR = 0.356, 95 % CI = 0.15–0.88), p = 0.014). We found that 66.7 % of the AA carriers had distant metastases whereas 81 % of the AG + GG carriers were free from metastases ($\chi 2$ = 10.2, p = 0.006). Genotyping for the IL-17F T7488G SNP revealed no significant differences in genotype distribution between cases and controls. However, we found a tendency for shorter median survival (19,9 months) of the heterozygous CT carriers compared to the TT genotype (p = 0.129).
Conclusion: Conclusively, we might suggest that heterozygosity for the IL-17A G197A might have a protective role in CRC development and metastatic behaviour.

PS-10-004
mRNA gene expression analysis by quantitative PCR in residual liquid-based Pap test
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Objective: to evaluate the possibility of differentiation CIN 2+ from CIN1 or less (normal epithelium/benign tissue changes of the cervix) in the residual liquid-based Pap test CellPrep media based on the expression of the 21-gene panel mRNA measurement by quantitative PCR
Method: mRNA expression of the 21 genes (Ki-67, STK-15, CCNB1, CCND1, MYC, MYBL2, P16INK4A, PTEN, BIRC5, BCL2, BAG1, TERT, NDRG1, ESR1, PGR, HER2, GRB7, MGB1, MMP11, CTSL2, CD68) was measured by quantitative PCR in the residual media from the vial after Pap-test CellPrep from 81 women within 3 months of the obtaining the histological examination
Results: We discovered that combined evaluation of the 21 gene expression panel allows, according to the discriminant analysis, to carry out the correct classification for 49 patients in the group CIN 2+ in 100 % of cases, and for the group CIN1 or less (32 patients) in 96.88 %. It was 1 (1.23 %) false positive case for glycogen dystrophy changes. The total percentage of the predicted classifications is 98.77 %. The correct classification is mainly influenced by the estimation of the expression of 11 genes
Conclusion: The addition of the expression analysis of 21 gene panel by quantitative PCR to the Pap test CellPrep could be helpful in detecting severe cervical lesions.

PS-10-005
SPOP mutations and relationship with ERG rearrangement and PTEN loss in prostate cancer
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Objective: SPOP targets ERG for ubiquitin-proteasome degradation. SPOP mutations are associated with increased substrate levels. SPOP is mutated in prostate cancer (PrCa) and this seems to be mutually exclusive with ERG rearrangements. PTEN loss is often associated with ERG rearrangements. The objective of this study is to analyze the relationship of ERG rearrangements and PTEN loss with SPOP mutations.
Method: ERG rearrangement, PTEN loss and SPOP mutations were analyzed in 156 (76 FFPE and 80 frozen) PrCa (Parc de Salut MAR-Biobank, Barcelona, Spain) by immunohistochemistry, qPCR and direct sequencing. Pearson Chi-Square or Fisher's Exact test were used for categorical variables.
Results: ERG rearrangement was detected in 92 (59 %), PTEN loss in 61 (39.1 %) and SPOP mutations in 10 (6.4 %) samples. SPOP mutations are associated with ERG-wt tumours (15.6 %; $p < 0.0001$). Three of 15 (20 %) ERG-wt/PTEN-loss and 7 of 49 (14.3 %) ERG-wt/PTEN-wt tumours harbored SPOP mutations (p = 0.681). None GS = 6, 6 of 72 (8.3 %) GS = 7, and 4 of 48 (8.3 %) GS ≥ 8 tumours harbored SPOP mutations.
Conclusion: SPOP mutations are higher in GS ≥ 7 tumours (N.S.), and are associated with non-ERG rearranged PrCa, but not with PTEN status. SPOP alterations represent an alternative, ERG-wt, pathway. (FIS/ Carlos III/ FEDER/ PI15/00452, Spanish Ministry of Health).

PS-10-006

Molecular analysis of Brenner tumours reveals recurrent amplifications in malignant tumour variants

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Objective: Brenner tumour are rare, mostly benign, ovarian tumours. With rare incidence borderline and malignant variants are also reported. The histological appearance of these tumours is well described, but little is known about the underlying genetic defects in these tumours.

Method: We employed targeted next generation sequencing applying a 409 gene panel to analyze the mutational landscape in a cohort of 19 cases comprising 23 Brenner tumour variants and validated results by fluorescence in-situ hybridization (FISH), and quantitative PCR-based copy number assays. Additionally, we analyzed the TERT promotor region by conventional Sanger sequencing.

Results: In 6 % of the analyzed genes we identified 25 different point mutations. Forty-four percent of these mutations occurred in genes involved in cell cycle control and DNA repair or in epigenetic regulation processes. Copy number analysis revealed recurrent amplifications of the MDM2 gene in 75 % of the malignant cases, one case additionally harbored amplification of CCND1. No mutations were observed in the TERT promoter region.

Conclusion: In conclusion, although our approach was unable to identify the common genetic origin of benign BT we were able to highlight some associations with urothelial/transitional cell carcinomas on the genetic level providing a basis for further studies of Brenner tumours.

PS-10-007

Comprehensive MET mutation profiling by anchored multiplex PCR and next-generation sequencing

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Objective: Deregulation of the proto-oncogene, MET, confers an aggressive phenotype in a variety of human cancers and can be driven by gene amplification, overexpression, exon 14 skipping, gene fusions and kinase-activating point mutations. MET mutation profiling is important, as the various mutated forms of MET exhibit unique drug sensitivities. We developed targeted NGS assays based on Anchored Multiplex PCR (AMP™) to detect all types MET mutations from a single sample.

Method: AMP uses molecular barcoded adapters and single gene-specific primers for amplification, enabling open-ended capture of DNA and cDNA fragments. This allows for sequence identification of known and unknown mutations, including novel fusions, as well as copy number and expression analysis from DNA and RNA, respectively.

Results: We demonstrate the ability of AMP-based NGS to identify novel fusion partners for MET, including HLA-DRB1, CTTNBP2, and GTF2I in RNA extracted from FFPE samples. Furthermore, AMP enables NGS-based detection of MET amplifications in DNA and overexpression in RNA. Finally, AMP-based NGS detects exon 14 skipping and driver splice site mutations, as well as kinase-activating point mutations.

Conclusion: These results demonstrate that AMP-based NGS detects all types of MET mutations, enabling comprehensive characterization of MET deregulation from low-input clinical samples.

PS-10-008

The development of a 13-gene panel to early detect oral squamous cell carcinomas evaluating quantitative DNA methylation by bisulfite next generation sequencing

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Objective: Oral squamous cell carcinoma (OSCC) is usually diagnosed in an advanced stage, which is associated with worse prognosis. Here we describe a reliable method to early detect OSCC evaluating DNA methylation of 13 genes starting from oral brushing.

Method: 25 consecutive OSCC, 5 HG-SIL and their normal contralateral mucosa, 20 LG-SIL, 12 OLP and 40 healthy donors were included in this study. A Bisulfite-NGS approach evaluating 19 genes in parallel using MiSEQ (Illumina) was used for quantitative DNA methylation analysis including 355 CpGs. Bioinformatic evaluation was done by BSPAT, BISMA and Methylation Plotter tools.

Results: ZAP70, ITGA4, KIF1A, PARP15, EPHX3, NTM, LRRTM1, FLI1, MIR193, LINC00599, PAX1, MIR137HG MIR296, TERT, and GP1BB resulted epigenetically altered comparing OSCC vs normal healthy donors and contralateral mucosa. DNMT1, TERC, H19, LINE1 were found to be unchanged. ROC curve analysis identified the most informative 13 CpGs allowing us to create an algorithm of choice for early detection of OSCC/HG-SIL. All OSCC/HG-SIL and none of the normal donors resulted positives (AUC: 1); 5/30 normal distant mucosa, 16/20 LG-SIL and 2/12 OLP exceeded the threshold value.

Conclusion: Our bisulfite-NGS based assay could contribute to reduce the OSCC burden with its early diagnostic potential starting from a minimally invasive collecting procedure.

PS-10-009

Overexpression of ETS genes (ERG, ETV1, ETV4 and ETV5) in prostate cancer

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Objective: More than 90 % of ERG-overexpressing PrCa harbor a TMPRSS2-ERG fusion. TMPRSS2 is less often fused to other ETS members as ETV1, ETV4 and ETV5. The objective of this study is to analyze the expression of these genes and their relationship with prognosis in PrCa.

Method: ERG, ETV1, ETV4 and ETV5 mRNA expression was analyzed by qPCR in 65 PrCa and 3 non-neoplastic prostate samples (Parc de Salut MAR-Biobank, Barcelona, Spain). GADPH was used as internal control. Overexpression cut-off based on non-neoplastic prostate samples was ≥ 2.2.

Results: Forty-nine tumours (75.4 %) showed ETS gene overexpression. ERG, ETV1, ETV4 and ETV5 overexpression was detected in 58.5 , 23 , 7.7 and 4.6 %, respectively. Forty tumours (61.5 %) overexpressed only one ETS gene, and 9 cases (13.8 %) more than one. Single ETS overexpression was found in 84.6 % GS = 6 and 55.8 % GS $\geq$ 8 PrCa ($p = 0.055$). Only 7/38 (18.4 %) cases with ERG overexpression showed also other ETS genes with high levels.

Conclusion: Overexpression of ETS genes is a very frequent event in PrCa, ERG is the most frequently overexpressed, mainly as a single event. Single ETS gene overexpression showed a trend to be statistically associated with low grade PrCa. (FIS/ Carlos III/ FEDER/PI15/00452, Spanish Ministry of Health).

PS-10-010

Laboratory errors in the diagnostic process of RAS testing in Europe

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Objective: External quality assessment schemes evaluate RAS testing performance for therapy decisions in colorectal cancer. In the 2016 scheme, 69 % of laboratories participated successfully. This study aimed to evaluate the type and frequency of laboratory errors, provide feedback, and assess the improvement in 2017.
Method: A survey was sent to 51 laboratories with minimum one genotyping error (false-positive, false-negative result, wrong mutation) or technical failure during the 2016 scheme. Twenty-one laboratories (43 %) from 14 countries responded, yielding 33 errors for analysis.
Results: The participants reported both pre- (36.4 %), post- (33.3 %) or analytical (30.3 %) problems. Pre-analytical errors were mostly related to the DNA amount or quality extracted from the tissue (83 %), compared to analytical methodological or technical problems (each 30 %) and post-analytical interpretation errors and clerical errors (each 46 %). Different corrective actions and responsible persons were reported depending on the error cause. Based on these results, a workshop was organized with information on every test phase to provide feedback to laboratories. The remaining hurdles to overcome problems reported by the attendees were time and staff constraints (8/10) or organizational barriers (5/10).
Conclusion: Errors were observed at different test phases. Improvement of RAS testing and the effectiveness of measures will be evaluated during the next schemes.

PS-10-011

Onionin A, a compound isolated from onions, impairs tumour progression and lung metastasis in tumour-bearing mice by suppressing the protumoural functions of myeloid cells

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Objective: Tumour-associated macrophages (TAMs) and myeloid-derived suppressor cells (MDSCs) exhibit protumoural functions in tumour microenvironment. We evaluated the activity of a new compound isolated from onions, named onionin A (ONA), whether it inhibits protumoural functions of TAMs and MDSCs.
Method: ONA is a new sulfur-containing compound isolated from acetone extract of onion bulbs. Its activity on myeloid cells was evaluated in vitro and in vivo.
Results: ONA inhibited macrophage polarization toward M2 phenotype as well as the immunosuppressive activity of MDSCs by suppressing the activation of signal transducer and activator of transcription-3. Oral administration of ONA in tumour-bearing mice produced by the injection of LM8 mouse osteosarcoma cells significantly suppressed both subcutaneous tumour development and lung metastasis. Increased number of CD4- and CD8-positive lymphocytes in tumour tissues by ONA administration was found. In a coculture analysis of CD4- or CD8-positive lymphocytes and isolated MDSCs, ONA improved lymphocyte proliferation by suppressing MDSC activity. Furthermore, ONA impaired tumour cell proliferation in a coculture analysis of LM8 osteosarcoma cells and macrophages by suppressing protumoural functions of macrophages.
Conclusion: ONA showed a strong inhibitory effect on the protumoural functions of TAMs and MDSCs. ONA may be a potential new tool for antitumour therapy.

PS-10-013

PI3K/AKT/mTOR pathway members and eukaryotic translation initiation factors as new biomarkers in liver cancer

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Objective: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide. The initiation of protein translation is an important rate-limiting step in eukaryotes, and is crucial in the pathogenesis of many viral infections. Eukaryotic translation initiation factors (eIFs) are proteins that are involved in the initiation step of protein translation and are linked to the phosphatidylinositol-3-kinases (PI3K)/AKT/mTOR pathway. We investigate the role of eIFs and mTOR pathway members in HCC.
Method: We investigated the immunohistochemical expression of the eIF subunits 2α, 3C, 3H, 4E, 5 and 6 in 235 cases of virus-related human HCCs. Immunoblot analysis was also performed to address the expression of eIFs and mTOR pathway members in HBV- and HCV-associated HCC, HCC without a viral background, alcoholic livers and Wilson's disease.
Results: pmTOR, mTOR, pPTEN, PTEN and pAKT showed a significant increase in HBV- and HCV-associated HCC, chronic hepatitis B and HCC without a viral background. The eIF subunits p2α, 2α, 3B, 3D, 3 J, p4B, 4G and 6 were upregulated in HCV-associated HCC. Regarding eIF2α, peIF4B, eIF5 and the eIF3 subunits B, D, H, I and J, we noted a significant increase in HBV-associated HCC. HCC without viral background displayed a significant increase for the eIF subunits p2α, 3C, 3I, 4E and 4G.
Conclusion: These results demonstrate that mTOR members and eIFs play a crucial role in translational control in chronic hepatitis B and C, HBV- and HCV-associated HCC and non-virus related HCC and therefore serve as novel biomarkers.

PS-10-014

Targeted next generation sequencing identifies HER2 status of breast cancer patients

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Objective: About 15-20 % of breast cancer patients harbor amplification of the HER2/ERBB2 gene accompanied by overexpression of HER2. Current guidelines for assessing the HER2 status in breast cancer demand investigation of protein expression by immunohistochemistry (IHC) and for equivocal cases determining HER2 gene amplification by in-situ hybridization (ISH). Studies interrogating the feasibility of targeted next generation sequencing (NGS) for determination of the HER2 status are still limited.
Method: We performed targeted NGS applying breast cancer specific gene panels on 35 Her2 equivocal cases with full pathological work-up including ISH and IHC.
Results: Assay validation for the detection of the HER2 status was performed by analyzing breast cancer samples with clear positive ($n = 4$) and clear negative results ($n = 6$) yielding a concordance rate of 100 %. Thirty-five cases were equivocal by IHC with 7 cases showing amplification by ISH. We confirmed all non-amplified cases as HER2-negative and corroborated all but one of the equivocal cases as HER2 amplified. Concordance between the gold standard and NGS was 97.8 % (sensitivity 90.9 %, specificity 100 %). Furthermore, genetic events in other drivers were identified.
Conclusion: In conclusion, targeted NGS can be used to determine the HER2 status with high specificity and high concordance with gold standard methods, and identifies additional genetic events.

PS-10-015

Apolipoproteins genes expression is dysregulated in colorectal adenocarcinoma

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Objective: Apolipoproteins (APOs) are molecules involved in several metabolic conditions and disorders, including colorectal cancer (CRC). This study aimed to determine APOA1, APOB, APOC3 and APOE expression levels among CRC subjects.
Method: Expression levels of APOA1, APOB, APOC3 and APOE genes were determined using RT-PCR, Sybergreen based, in 56 colorectal adenocarcinoma biopsies.
Results: In this work, we found an upregulation of APOB, and APOE between tumour and normal tissues, with a mean 10-fold increase in tumours ($p < 0.0001$). On other hand, APOA1 and is downregulated among tumour tissue, with 5-fold decrease in tumours ($p < 0.001$).
Conclusion: Our results show that lipid metabolism is disrupted in CRC, tumour cells seem to have higher LDL concentration by upregulation of APOE and APOB genes, and low levels of HDL by APOA1 gene downregulation. These findings validate the potential role of lipid metabolism genes in CRC progression.

PS-10-016

Proinflammatory cytokine polymorphic variants are associated with colorectal adenocarcinoma

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Objective: Cytokines are the main mediators of immune responses, and intestinal inflammation early stages are not elucidated. This study aimed to explore the impact of pro-inflammatory IL-1, IL-2, IL-12, TNF-α, and IFN-γ common polymorphisms in Colorectal Adenocarcinoma (CRAC).
Method: CRAC 56 biopsies and 100 blood samples/ healthy subjects control group were submitted to IL1A -889 T>C, IL1B (-511C>T, and +3954C>T), IL1R (Pst1970C>T), IL2 (−330 T>G, and +160G>T), IL12 (+1188C>A), TNFA (−238G>A, and −308G>A), and IFNG (+874 T>A) polymorphisms were genotyped/ commercially available kits.
Results: High expression alleles of IL1A −889 T (OR = 0.3; 95%CI:0.1–0.6), IL1B −511C (OR = 0.4; 95 % CI:0.2–0.7), TNFA −238A (OR = 0.5; 95 % CI:0.3–0.9), TNFA −308A, IL−2 + 160G (OR = 0.5; 95 % CI:0.3–0.9), and IL12 + 1188A (OR = 0.3; 95 % CI:0.1–0.6) associated with CRAC prevalence ($p < 0.002$).
Conclusion: Potential pathogenesis of proinflammatory cytokine polymorphisms in CRAC predispose prognostic appear to have important role/ uncontrolled inflammatory responses in genetic epithelial remodelling.

PS-10-017

Introduction of an EQA scheme for ROS1, RET and MET testing in lung cancer

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Objective: UK NEQAS for Molecular Genetics provides an EQA scheme for the testing of EGFR, ALK, KRAS, BRAF, and PIK3CA in lung cancer. Laboratories are now required to test for the additional biomarkers ROS1, RET and MET. To support laboratories in fulfilling these requirements, UK NEQAS for Molecular Genetics has provided an EQA scheme for these genes.
Method: Since 2015 four rounds of EQA have been provided. Participants were supplied with formalin fixed paraffin embedded (FFPE) material and required to test for any or all of the following: rearrangements in ROS1 and/or RET; copy number alterations in MET using their usual testing method. Laboratories were required to report results in their usual reporting format and interpret in the context of the clinical scenario supplied.
Results: Participation has almost doubled over the four EQA rounds. ROS1 was the most frequently tested gene with FISH being the most common testing method. More than a third of laboratories performed testing using either RNA-based methods or NGS. Errors were reported in the testing of ROS1 and RET in more than one EQA round.
Conclusion: The identification of erroneous results in testing highlight the need to provide an EQA scheme for the testing of additional biomarkers in lung cancer.

PS-10-018

PD-L1 expression does not correlate with EGFR/ALK/ROS1 status in pulmonary adenocarcinomas

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Objective: PD-L1 immunohistochemistry selects patients for anti-PD-L1 immunotherapy, although controversy exists actually due to low accuracy of PD-L1 scoring/immunohistochemistry staining. This biomarker runs together with EGFR/ROS/ALK status for target therapy. A series of 55 cases of pulmonary adenocarcinomas with Molecular Pathology determinations after clinicians demanding had PD-L1 (22C3 DAKO) immunostainning.
Method: PD-L1 immunoexpression was correlated with EGFR (exons 19 and 21) and ALK and ROS1 status. EGFR mutations were search by Sanger sequencing and ALK/ROS1 status were assessed by FISH (ZytoLight SPEC ALK/EML4 Tricheck and ZytoLight SPEC ROS1 Dual Color Break Apart Probe FISH assay, respectively).
Results: From the PD-L1 positive cases (>1 % - 19), one case (5 % positive cells) had EGFR L858R mutation. All cases were ALK and ROS1 negative. From the 36 negative PD-L1 cases, 5 presented EGFR E746_A750/L858R mutations.
Conclusion: This work showed no concomitance between PD-L1 and EGFR, ALK or ROS1. Thereby more studies are needed to infer about PD-L1 and other genes status to identify patients who will benefit from anti-PD-1/anti-PD-L1 therapy or other therapy management.

PS-10-019

Improving DNA quality from formalin-fixed paraffin-embedded tissue extraction for next-generation sequencing applications

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Objective: To ensure DNA samples submitted into the UK 100,000 Genomes Project can deliver high quality whole genome sequencing (WGS), UK National External Quality Assessment Service (NEQAS) for Molecular Genetics with NHS England have developed an external quality assessment (EQA) scheme for the quality of DNA extracted from formalin-fixed paraffin-embedded (FFPE) tissue.
Method: Laboratories providing FFPE derived DNA samples for WGS have participated in three EQAs, each providing three FFPE tissue samples for DNA extraction. The DNA samples were analysed by UK NEQAS for a range of quality metrics including volume, DNA mass,

260/280 ratio, fragmentation and quality of Next Generation Sequencing library preparations . An overall score for DNA quality was generated and laboratories were bench-marked against each other.
Results: EQA results demonstrated a high variation in DNA quality through a range of DNA extraction methodologies. Review of processes and continued EQA participation showed marked improvement in the quality of DNA.
Conclusion: These EQAs highlighted extraction methodologies used for routine molecular pathology applications were not suitable for WGS. Application of quality metrics, inter-laboratory bench-marking and continued participation allowed laboratories to identify and address problems efficiently and effectively to improve the quality of the DNA extracted for sequencing.

PS-10-020
Molecular profiles of thyroid cancer: Classification based on features of tissue revealed by mas spectrometry imaging
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Objective: Currently, classification of thyroid cancer based on histopathological features could be supported by molecular biomarkers, including markers identified with the use of high-throughput "omics" approaches.
Method: We aimed to characterize molecular profiles of different thyroid malignancies using mass spectrometry imaging which enables the direct annotation of molecular features with molecular pictures of an analyzed tissue. Fifteen formalin-fixed paraffin-embedded tissue specimens corresponding to five major types of thyroid cancer were analyzed by MALDI-MSI after in-situ trypsin digestion, and the possibility of classification based on the results of unsupervised segmentation of MALDI images was tested.
Results: Novel method of semi-supervised detection of the cancer region of interest (ROI) was implemented. We found strong separation of medullary cancer from malignancies derived from thyroid epithelium, and separation of anaplastic cancer from differentiated cancers. Reliable classification of medullary and anaplastic cancers using an approach based on automated detection of cancer ROI was validated with independent samples. Moreover, extraction of spectra from tumour areas allowed the detection of molecular components that differentiated follicular cancer and two variants of papillary cancer (classical and follicular).
Conclusion: We concluded that MALDI-MSI approach is a promising strategy in the search for biomarkers supporting classification of thyroid malignant tumours.

PS-10-022
Quality improvement project to reduce the failure rate of KRAS mutation molecular tests
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Objective: Confirm and investigate audit data identifying higher-than-expected KRAS mutation test failures on colorectal cancer specimens, aiming for 100 % success in KRAS mutational status testing.
Method: Electronic patient record retrieved all KRAS molecular tests on colorectal cancers over 11-month period. In-depth analysis was performed on all test fail cases and sample of control 'success' cases. Data collected included specimen and tumour type, use of neoadjuvant therapy and date/day of end-to-end specimen pathway stages (operation, arrival in laboratory, cut-up), to calculate total days in fixative. Key observations were discussed by gastrointestinal histopathology team.
Results: 27/152 (17.8 %) KRAS molecular tests on colorectal cancers failed: 'Next Generation Sequencing analysis could not be performed due to insufficient library concentration… probably due to DNA quality'. Key observations: 78 % fail and 5 % control cases processed on Fridays; 56 % fail and 15 % control cases fixed ≥ 6 days. Were fixative type and/or prolonged fixation affecting DNA quality? The fixative was changed from 10 % formal saline to 10 % neutral buffered formalin, and KRAS molecular tests prospectively monitored. KRAS molecular test failure rate was 0/103 (0 %) over the next 12 months.
Conclusion: We strongly recommend the routine use of neutral buffered formalin over formal saline as specimen fixative, especially when using ancillary molecular testing.

PS-10-023
Evaluation of new rapid fluorescence in situ hybridisation reagents on Formalin Fixed Paraffin Embedded (FFPE) and cytological specimens: A comparison study
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Objective: Fluorescence in situ Hybridization (FISH) is a commonly used testing modality in the modern clinical anatomic pathology laboratory. However, as it typically takes 16–24 hrs, faster protocols are needed. The purpose of this study was to compare the use of new rapid FISH reagents available from Abbott and Dako/Agilent on a set of 100 clinical specimens with regards to quality of FISH slides produced and workflow time.
Method: 50 FFPE and 50 cytological de-identified clinical specimens were tested by Abbott and Dako/Agilent FISH methodologies using 6 different probes. FISH slides were scanned on a fluorescence microscope and then scored in a blinded fashion on a 1 to 5 point scale with regards to nuclear morphology, signal intensity, background, signal specificity, and overall quality.
Results: The Abbott arm achieved higher overall slide quality scores on both the FFPE (4.4 vs 3.8) and cytological (4.8 vs 4.2) specimens. Overall protocol time was also shorter for the Abbott arm compared to the Dako/Agilent arm (3.4 hrs vs. 4.0 hrs).
Conclusion: Although both methodologies generated acceptable FISH slides in a fraction of the usual time, the Abbott arm resulted in better hybridization quality than the Dako/Agilent arm with a significantly shorter processing time.

PS-10-024
The analytical sensitivity for detecting T790M mutation in circulating tumour DNA of lung adenocarcinoma patients. Comparison of two methodologies
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Objective: The aim of this study was to determine the analytical sensitivity for detecting T790M mutation using two next generation sequencing technologies (Ion Torrent PGM and 454) on circulating tumour DNA (ctDNA) of lung adenocarcinoma patients.
Method: DNA extracted from plasma samples of 102 lung adenocarcinoma patients was PCR amplified. 56 cases were sequenced

using PGM and 46 using 454. The general sequencing artifact level and the artifact level specific for each nucleotide change were determined.
Results: Sequencing artifact level was higher in PGM compared to 454. The average noise level was 0.072 ± 0.797 % and 0.034 ± 0.616 %, and the 95th percentile was 0.238 % and 0.128 % in PGM and 454, respectively. In both methods the most common nucleotide changes were T>C and A>G. The analytical sensitivity was defined as the 95th percentile of C>T sequencing artifact level (0.18 % in PGM and 0.109 % in 454) because this is the nucleotide change seen in T790M mutation. Based on these analytical cut-offs, 27 (48 %) and 26 (56 %) cases were T790M positive in PGM and 454 groups, respectively. Across both methods 77 cases had duplicate testing with an agreement rate of 74 %.
Conclusion: Deep sequencing methods could be applied to identify low frequency point mutations in ctDNA.

PS-10-025
Translation initiation separates low and high grade and colon and rectum carcinoma
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Objective: Colorectal cancer (CRC) is the third most common cause of cancer related death worldwide. The step of initiation, regulated by eukaryotic initiation factors (eIFs), is assigned as rate limiting step in protein synthesis. eIFs become major targets for cancer therapy and are functionally linked to the PI3K/AKT/mTOR signaling . However, little is known about their contribution in CRC. Therefore, we aimed to investigate the role of eIFs and mTOR members in CRC.
Method: eIF and mTOR expression was analysed in primary low and high grade CC and RC samples in comparison to controls without any disease-related pathology on protein and mRNA expression. To assess the therapeutic potential of targeting eIFs, siRNA knockdown experiments in HCT116 cells were performed.
Results: Protein and mRNA levels of low grade and high grade CC and RC patients revealed a significant up-regulation of mTOR members and most eIF subunits. Reducing eIF1, eIF5 and eIF6 expression by inducible knockdown in the HCT116 cell line led to increased levels of free ribosomal subunits.
Conclusion: Various eIFs are altered; particularly eIF1, eIF5 and eIF6, in low and high grade CC and RC thus aberrant translation initiation might represent a novel mechanism in CRC carcinogenesis.

PS-10-026
Meta-analysis based miRNA signature discriminates cervical cancer from normal samples
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Objective: The aim of this study is to identify miRNAs, which are playing a part in progression of cervical neoplasia by a ranking based meta-analysis approach.
Method: Three mRNA and three miRNA expression studies, which include normal, CIN1, CIN3 and SCC samples were selected from Array Express and GEO databases. miRNA studies were combined with ANOVA dependent ranking based meta-analysis program to find out differentially expressed (DE) miRNAs that can discriminate CIN1, CIN3 and SCC samples from normal samples. The top ten DE miRNAs with the highest ranks in meta-list were selected and their predicted targets were identified by miRDB target prediction tool. mRNA datasets were used for miRNA-target validation and as a test dataset.
Results: Among the targets, 26 genes were found to be common with the DE genes between normal and SCC groups from two independent studies. Furthermore, they were used for classification of normal and SCC samples in an independent mRNA test dataset and they were able to classify these two groups with 100 % precision.
Conclusion: The meta-analysis results together with validation analysis of their targets may point out the potential roles of miRNAs as biomarkers for the diagnosis and prognosis of cervical cancer.

PS-10-027
Pre-analytical challenges during RAS testing: Tissue quality and the estimation of tumour cell percentage
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Objective: In addition to external quality assessment (EQA), laboratories need tailored feedback about improving biomarker testing practices. A workshop was organised to resolve issues related to the estimation of tumour cell percentage and tissue quality as part of a larger study on neoplastic cell content.
Method: Laboratories that failed the 2016 EQA scheme were invited to a workshop to improve RAS testing in Europe. An interactive course about tissue quality took place to stress the importance of the pre-analytical phase. During a microscopic session, five H&E stained tumour tissue slides were discussed and tumour cell percentages estimated. Participants included 4 pathologists, 3 molecular biologists, a technologist and a clinical geneticist from 6 laboratories.
Results: Tumour content is checked routinely by visual estimation by the pathologist in 89 % of the 6 laboratories. The average difference between the lowest and highest tumour content estimation was 31 %. The sample with the largest difference (40 %) was considered the most difficult due to inflammatory cell infiltration and necrosis. For non-pathologists this difference was even larger (60 %).
Conclusion: This workshop stressed the importance of the pre-analytical phase and provided feedback to the laboratories. Harmonizing tumour cell percentage determination is needed to improve biomarker testing and therefore, further research was initiated.

PS-10-028
Redox genes expression is down regulated in colorectal adenocarcinoma
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Objective: Oxidative stress plays an important role on colorectal cancer (CRC) development. Superoxide dismutase (SOD) and glutathione transferase (GPT) are are enzymes responsible for the detoxification of superoxide ROS. Although the action mechanisms of these enzymes in CRC is still uncertain. This study aimed to determine MNSOD, SOD3, GSTT1, GSTM1 and GSTP1 expression levels among colorectal cancer subjects.

Method: Expression levels of MNSOD, SOD3, GSTT1, GSTM1 and GSTP1 genes were determined using Real Time-Polymerase chain reaction, Sybergreen based, in 56 colorectal adenocarcinoma biopsies.
Results: We found significant differences in GSTs and SODs expression between tumour and normal tissues, with a mean 5-fold decrease in tumour tissues ($p < 0.01$). MNSOD gene showed (10-fold) the higher decrease ($p < 0.0001$), whereas GSTP1 have the lowest decrease with only a 2-fold decrease ($p < 0.05$) in tumour tissues.
Conclusion: Our results corroborate the potential role of oxidative stress in CRC development and provide insight into the potential pathogenesis of GSTs SODs in CRC predisposal. Furthermore, downregulation of genes involved in redox metabolism seems to be involved in tumour progression in CRC subjects.

PS-10-029
Structural-molecular disorders of endometrial receiptivity in infertile women, suffering from external genital endometriosis
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Objective: Study of structural and molecular disorders in endometrial receptivity in infertile women with external genital endometriosis (EGE).
Method: Morphological and mRNA studies of 94 women with EGE and infertility without combined genital pathology and 54 control woman were carried out. Immunohistochemically LIF, HOXA10, glycodelin A, integrin $\alpha v\beta 3$, estrogen and progesterone receptors, aromatase were studied. mRNA of the LIFR, LIF, ESR1, PGR, HOXA10, and PTEN genes was determined by RT-PCR.
Results: Patients with EGE have following particularities: 2.4 times decrease in the area occupied by pinopodes on the surface epithelium of the endometrium, a lower expression of the LIF (4.2 + 0.7 and 5.7 + 0.3 points Respectively), HOXA10 (1.8 + 0.4 and 4.0 + 0.4 points), integrin $\alpha v\beta 3$ (0.7 + 0.4 and 2.4 + 0.4 points), glycodel A (1.0 + 0.3 and 1.7 + 0.3 points) ($p > 0.05$), an imbalance in the expression of estrogen and progesterone receptors, an increase in aromatase expression (5.8 and 3.7 points), and a decrease in the expression of NOxA10 mRNA in 1.4 times ($p > 0.05$), LIF in 1.7 times ($p > 0.05$), progesterone Receptor in 1,6 times ($p > 0,05$), PTEN in 1,4 times ($p > 0,05$).
Conclusion: Infertility in endometriosis can be associated withstructural immaturity and molecular disorders in endometrium.

PS-10-030
RNA-based parallel sequencing and multiplex FISH are helpful for molecular subtyping of small round cell sarcomas. A study on 45 cases
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Objective: Small blue round cell sarcomas (SBRCS) form a heterogeneous group of clinically aggressive tumours. Due to their rarity and morphological overlap, the correct diagnosis is frequently challenging. Therefore, we aimed at investigating two multiplex methods for gene fusion detection on their utility in the diagnosis of SBRCS.
Method: 45 SBRCS were analyzed by RNA-based parallel sequencing (using Archer FusionPlex Sarcoma Kit covering 26 genes which are frequently involved in sarcoma-specific gene fusions) and various multiplex break apart/fusion FISH probes (ZytoVision).
Results: Parallel sequencing revealed gene fusions in 31 sarcomas, among them previously unrecognized CIC-DUX4 and BCOR-CCNB3 translocations as well as a potential novel rearrangement. By multiplex FISH fusions were detected in 27 SBRCS. Results were usually available after 3 days. Sequencing was feasible even with small and archival samples, and results were usually available after 6 days. Eleven SBRCS were negative for any gene fusion.
Conclusion: Multiplex FISH is a fast, effective and reliable method to confirm suspected fusions (based on morphology, IHC and/or sequencing). RNA-based parallel sequencing allows the detection of unknown or unexpected gene fusions and is feasible also on routine samples. Even after comprehensive investigation by FISH and sequencing 11/45 SBRC remained negative for any known rearrangement.

PS-10-035
High-density pile-up array is a reliable tool for the evaluation of high throughput screening in fluorescence in situ hybridisation
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Objective: Tissue microarrays are considered as a versatile tool for high-throughput screening. However, we devised the High-density Pile-up Array, which could arrange a specimen densely without sacrificing original tissue. In this study, we evaluated the high-density Pile-up Array by comparing staining results of two differently sized tissue cores.
Method: Sequentially, 126 Formalin-Fixed Paraffin-Embedded resection specimens of pulmonary adenocarcinoma were selected. From each block 0.1 mm section was obtained and 2–3 places (a normal part and tumour part) were punched-out. The size of the tissue core was 3.0 mm ×4.0 mm. High-density Pile-up Arrays were created with the following tissue core dimensions. Type A: 0.1 mm ×3.0 mm × 4.0 mm. Type B: 0.1 mm ×0.1 mm ×3.0 mm. From both types HPA specimens were prepared and stained by ALK IHC and FISH analysis.
Results: We could detect heterogeneity with type A. The total agreement rate of ALK IHC and FISH was 99, 7 % for Type A. In core size B, the observed cell count was less than 50 cells in all cores.
Conclusion: HPA is useful for high-throughput screening analysis of FISH and IHC. Examination of core size and sampling point in consideration of heterogeneity and disagreement are necessary.

PS-10-036
Glycoprotein asporin is associated with progression of high-grade but not of low-grade breast cancer
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Objective: Asporin plays important role in normal development, in particular of cartilage, bone and teeth. Although asporin can now be found in multiple cancer related studies, its role in breast cancer is not clear.
Method: Data mining was performed using the Kaplan-Meier Plotter and other databases. Migration and invasion of Hs578T, MDA-MB-231 and BT549 breast cancer cells was tested upon modulation of asporin. RNAscope in situ hybridization with asporin probe was performed on formalin-fixed paraffin-embedded tissues of invasive breast cancer.
Results: Data mining revealed that high asporin expression may serve as a good prognostic marker for tumour grades 1 and 2, while the opposite was observed in high-grade breast cancer. Another in silico analysis identified asporin expression in Hs578T cell line which we confirmed by qRT-PCR and immunoblotting. Downregulation by shRNA inhibited invasion of Hs578T through collagen type I matrix. Invasion of asporin-negative MDA-MB-231 and BT549 breast cancer cells through collagen type I was enhanced by recombinant asporin. In line with other studies, we have confirmed asporin expression by RNAscope in situ hybridization in cancer associated fibroblasts in invasive breast cancer.
Conclusion: Asporin expression was associated with progression of high-grade breast cancer which is supported by in vitro experiments with breast cancer cell lines.

PS-10-037

Diagnostic significance of microRNA-128 expression levels in malignant and benign breast tissues

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Objective: The investigation of miRNAs transcriptome unravels the potential for improvements in prognosis, diagnosis and monitoring of breast adenocarcinomas. The purpose of the present study was to evaluate the expression of miR-128 in 134 malignant and 67 benign breast tumours, in order to explore its differential diagnostic and prognostic value in breast cancer.
Method: Total RNA was extracted, polyadenylated and reversely transcripted from the tissue specimens analyzed herein. The end product was used in a highly sensitive real-time PCR protocol for the expression analysis of miR-128 and snoRNA RNU48, the latter of which served as a reference gene. Relative quantification analysis was performed by applying the 2-CT method, whilst the final step was a comprehensive statistical analysis.
Results: miR-128 expression was found to be significantly upregulated ($P = 0.004$) in malignant neoplasms of the breast in comparison to the benign tumours arising in the same site. Moreover, miR-128 levels showed the ability to accurately discriminate between cancerous and benign specimens, based on ROC curve analysis (AUC: 0.642; 95 % CI 0.532–0.732; $P = 0.004$).
Conclusion: According to our preliminary results, the expression of miR-128 could be regarded as a new promising indicator for the differential diagnosis between malignant and benign breast lesions.

PS-10-039

Chromogenic in situ hybridisation test for breast cancer patients with equivocal Her2Neu status: Experience of Salah Azaeiz Institute

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Objective: The aim of this study was to determine HER2 gene amplification; using the CISH method in breast carcinoma samples with equivocal Her/Neu status (IHC +2).
Method: This study was conducted from Mars 2014 to November 2016 using 205 consecutive equivocal Her 2/Neu status breast carcinoma samples. CISH simple probe assays (ZYTODOT SPEC HER2 probe Zytovision) were performed for all equivocal Her2/Neu samples using polyclonal antibody (NCL-L-B11 Novocastra). The stained slides (CISH and Her2/Neu) were interpreted referring to ASCO/CAP guideline.
Results: 152 (74, 15 %) cases among 205 equivocal Her2/ Neu breast cancer patients were not amplified by CISH. 53 specimens (25, 85 %) were amplified which 47 (88, 68 %(5 47/53))were weakly amplified and 6 (11,32 % (6/53)) cases strongly amplified.
Conclusion: In the literature, many studies report a high number of 2 + cases evaluated by IHC, in which amplification by CISH was not detected. A subset of these cases could involve chromosome 17 polysomy, which is frequently associated with IHC 2 + tumours. The dual core CISH could reduce this false positive rate. In other hand, a higher amplification rate by CISH was detected in studies that used monoclonal antibodies, compared to studies that used polyclonal antibodies. IHC 2 + tumours without gene amplification could indicate that at least some of these cases were either "overstained" or "overread" in IHC analysis. Using former FDA-approved criteria for HER2 interpretation, utilizing non-validated kits, and lack of any quality assurance program. Therefore, following the new 2014 ASCO guideline and comprehensive quality assurance should be implemented to ensure accuracy of HER2 testing.

PS-10-042

Immunohistochemical analysis of PD-L1 expression in malignant melanomas and melanocytic nevi

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Objective: Control receptor PD1 (programme death cell protein) is expressed by activated T lymphocytes during inflamation, autoimmune and tumour processes. PD1 is connected with ligands (PD-L1, PD-L2) expressed by stromal cells, tumours and regulatory T cells (Tregs), which decrease immune reactions in tumour microstromal environment. Interaction PD1/PD-L1 restrict lymphocytes activities and antitumour immune reactions. It facilitates growth of tumour cells.
Method: We tested 83 malignant melanomas devided into four groups accroding to deep of invasion and 25 benign pigmented nevi. From formalin fixed and paraffin embedded tissues was performed 5 μm thick samples coloured in immunoautomaton VENTANA, incubated 20 min with primary rabbit monoclonal antibody PD-L1 and DAB (diaminobenzidine) as chromogen. Density of PD-L1 positive melanocytes and lymphocytes was evaluated in light microscope in area 1 mm2 in "hot spot" regions in center and periphery of lesions.
Results: We found out significant differences in density of PD-L1 expression in observed cells. Observed expression was negative in nevi.
Conclusion: Analysis demostrates increasing of PD-L1 expression especially in melanocytes and stromal lymphocytes in advanced stages of malignant melanomas, in comparison with earlier stages. We expect PD-L1 positive lymphocytes cooperate with melanocytes during growing phase of melanomas.

PS-10-043

Optimisation of tumour markers panel for colorectal circulating cancer cells detection

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Objective: Currently, tumour staging procedures as well as modern imaging techniques lack in sensitivity to detect micro-metastases. Therefore, highlighting and even monitoring the tumour cells dissemination might be crucial for the prognosis improvement in patients with high risk of metastatic relapse. In this view, our study aims to validate a tumour marker panel for the detection and count of colorectal cancer circulating cells in the peripheral blood.
Method: HT-29 colorectal adenocarcinoma cell line was used for the in vitro screening of the tumour expression markers. For the analysis, cells were detached from the cell culture surface, treated with Fix&Perm solutions and stained over night with EpCam-FITC, Her2-PerCP Cy5.5, EGFR-APC, panCK-AF647, c-MET-AF700, MUC-1-AF750 and Sox2-PB antibodies. The acquisition and analysis of the samples was performed using a Beckman Coulter Gallios cytometer and Beckman Coulter Gallios Software.
Results: Our results show that HT-29 cells strongly express EpCam, panCK and MUC-1 and lack the expression of c-MET and Sox2. On this basis, HT-29 cells were detected and counted after their spike into peripheral blood samples.
Conclusion: Flow cytometry could be used for medium and long term monitoring of the colorectal circulating cells number, based on their EpCam, panCK and MUC-1 expression.

Monday, 4 September 2017, 09:30–10:30, Hall 3
PS-11 Ophthalmic Pathology

PS-11-001
IgG4-related disease and non-Hodgkin lymphoma: A temporal spin
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Objective: IgG4-related disease (IgG4-RD) is a fibro-inflammatory condition which induces organ expansion, specific histological findings—storiform fibrosis, obliterative phlebitis and plasmacytic IgG4+ infiltrates—and higher risk of malignancy. We report a case of orbital IgG4-RD following a lymphoma diagnosis.
Method: A 62 year-old male presented with ocular pain and progressive vision loss. Imaging studies showed ciliary body thickening; subsequent biopsies revealed a non-Hodgkin lymphoma of small mature B-cells, with Igκ monoclonality. The patient underwent ocular radiotherapy. Nevertheless, 2 years later, eye enucleation was performed due to inexorable orbit enlargement.
Results: Grossly, a white-yellow lesion expanded both sclera and choroid. Microscopically, we observed storiform fibrosis, an intense T-lymphocyte infiltrate with germinal centers and numerous plasma cells, displaying conserved κ/λ ratio and >50 IgG4+ cells/HPF, supporting the sclerosing pseudotumour (IgG4-RD) diagnosis. Further investigation unveiled increased serum IgG4 and retroperitoneal fibrosis, confirming an IgG4-RD.
Conclusion: The presentation of IgG4-RD as ocular pseudotumour is rare, especially in the sclera, since the majority affect the lacrimal gland and periorbital soft tissue. We present the second case of IgG4-RD following radiotherapy for lymphoma, illustrating an inversion in the presentation timing so far described. In our regard, this patient in fact suffered from underlying—yet undiagnosed—IgG4-RD with a superimposed lymphoma.

PS-11-002
Massive retinal gliosis masquerading as an intraocular tumour
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Objective: Massive retinal gliosis is a rare, pseudoneoplastic glial proliferation that may develop in association with congenital malformations or trauma. Some are syndrome associated with entities such as neurofibromatosis type 1 or tuberous sclerosis. Herein, we report the clinicopathological features of a massive retinal gliosis case in a 23-year-old male patient.
Method: The surgical specimen was routinely processed by formalin fixation and paraffin embedding. Hematoxylin and eosin staining and immunohistochemical tests were performed.
Results: : Histologic examination revealed the replacement of the anterior and posterior ocular compartments with a proliferation of interweaving bundles of spindle-shaped cells with uniform nuclei and delicate fibrillary cytoplasm. Mitotic figures were rare. Thick-walled, hyalinized blood vessels, microcystic spaces and the occasional presence of Rosenthal fibers were observed. The process was accompanied by focal calcifications, calcospherites and osseous metaplasia. A particular feature was the adipose tissue infiltration of the central area. Immunohistochemistry was positive for glial fibrillary acidic protein, vimentin and S-100 protein. Additionally, moderate diffuse staining for Melan-A and Ki-67 < 3 % were observed.
Conclusion: The aforementioned features are consistent with massive retinal gliosis, a pseudoneoplastic reactive process developed on a congenital malformation. This rare condition raises differential diagnosis issues with malignant melanoma and schwannoma.

PS-11-003
Ocular Pathology: A glance over 10 years of institutional experience
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Objective: Hospital de Santa Maria (Lisbon, Portugal) is a tertiary healthcare institution with an experienced Ophthalmology Department. We present our expertise through a 10 year-long series.
Method: Retrospective data pertaining to the 2007-2016 period were evaluated for the following criteria: age, sample type, location and pathology.
Results: A total of 661 reports were assessed, increasing from 41 in 2007 to 103 in 2016. Age ranged from 1 month to 93 years. The accounted procedures were excisional biopsies (75 %), incisional biopsies (21 %) and enucleations (4 %). The predominantly involved anatomical structures were palpebral skin (37 %), conjunctiva (25 %) and cornea (14 %). In the 419 cases remaining after cutaneous palpebral pathology was excluded, the majority were inflammatory/reactive changes (37 %), neoplasms (36 %) and the remainder consisted mostly of degenerative conditions (18 %); malignancies (20 %) were led by squamous cell carcinoma (6 %), primarily from the conjunctiva (85 %); regarding melanoma (5 %), 53 % originated in the uvea; melanocytic nevi (8 %) prevailed among benign neoplasms (16 %). Particularly noteworthy were the unique diagnosis of metastatic prostatic and lung carcinoma, and an IgG4-related disease.
Conclusion: Throughout the 10-year this series comprises, the specimens have almost tripled in number. To our knowledge this is the only retrospective study that encompasses all the ocular pathologies in one institution.

PS-11-004
Ciliary body medulloepithelioma in an adolescent girl: Report of a case
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Objective: Ciliary body medulloepithelioma (CBME) is a rare congenital neoplasm usually presenting in young children, with very few cases described in adolescents. Its rarity and clinical presentation may contribute to a delay in diagnosis. We report a case of a CBME with an aggressive clinical course that presented during adolescence.
Method: The clinicopathological features of a case of CBME are described, with a review of the literature.
Results: A 16-year-old female with a history of right eye enucleation for glaucoma was referred to our institution, with a rapidly growing 7 cm cranial invading orbital mass. The histopathological diagnosis of the enucleation specimen was unavailable at the time and a biopsy was performed. A small blue cell tumour was identified, and a diagnosis favoring PNET was rendered. After a partial response to chemotherapy, she underwent orbital exenteration. An embryonal tumour with neuroblastic and epithelial elements consistent with medulloepithelioma was observed. The enucleation specimen arrived 2 months later for review, and a diagnosis of teratoid CBME with poor prognostic features was confirmed.
Conclusion: CBME is rare neoplasm that can pursue an aggressive clinical course. Awareness of the entity, which may occur even during adolescence, could aid in its prompt diagnosis and to plan adequate treatment and follow-up.

PS-11-005
A rare case of ocular melanoma onset in a patient with vitreous hemorrhage
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Objective: Ocular melanoma is the most frequent eye tumour found in adult patients. This paper highlights a case of a small primary choroidal melanoma with particularly unusual clinical onset: vitreous hemorrhage.

Method: The patient presented with blurred vision in the right eye. Clinical examination and additional testing indicated a choroidal melanoma. Following surgical enucleation of the affected eyeball, on gross examination we identified a black dome-shaped structure with firm consistency, gripped to the posterosuperior wall side of the eye, with no invasion of the sclera or the optic nerve.
Results: Conventional hematoxylin-eosin stain examination found tumour cells of different sizes, sometimes intensely pigmented. At higher magnification, they shown to be type B spindle shaped cells, with a low mitotic index of 1 atypical mitose/mm2.
Conclusion: Vitreous hemorrhage as a primary event is uncommon for early choroidal melanoma and can be often misdiagnosed. This fact is usually seen only in cases when the melanoma has erupted through the Bruch membrane. Ocular spindle cell melanoma generally has a better prognosis than epithelioid cell melanoma. The reduced number of atypical mitosis, the absence of optic nerve and sclera infiltration and the lack of metastases are also predictive for good prognosis of the patient.

PS-11-006
Mammary Analogue Secretory Carcinoma (MASC) of the lacrimal gland: First case report
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Objective: Neoplasms of the lacrimal gland are classified similarly to those in the salivary glands; however, mammary analogue secretory carcinoma (MASC) of the lacrimal gland has not been reported so far.
Method: ETV6 break-apart FISH was used to confirm the diagnosis.
Results: The tumour presented in 28-year-old Asian man with a progressively worsening foreign body sensation, irritation, right upper lid swelling, blurred vision and diplopia. Imaging revealed a circumscribed heterogeneous lacrimal fossa mass. The lesion was surgically removed with no adjuvant treatment. Grossly the mass was oval, purple, and measured 3.5 cm in maximum diameter. It was partially cystic with brown fluid and variegated red-brown solid areas. Microscopically, the tumour had a predominantly papillary-cystic architecture with areas of solid and microfollicular pattern as well as vacuolated and clear cells. It was surrounded by a fibrous capsule which was variably infiltrated by islands of tumour cells. Immunohistochemistry was positive for S100, mammaglobin, and GCDFP15. Break-apart FISH analysis showed the presence of ETV6 translocation on chromosome 12.
Conclusion: MASC was described for the first time in 2010 by Skalova et. al. The recently published fourth edition of the WHO Classification of Head and Neck Tumours includes MASC in the chapter of secretory carcinoma of the salivary glands. We report the first instance of this neoplasm in the lacrimal gland.

PS-11-007
Mesectodermal leiomyoma of the anterior choroid: A case report and literature review
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Objective: To present one case of ocular mesectodermic leiomyoma and review the literature published over the past 20 years.
Method: A 69-year-old male presented with a solid tumour in the left eye's temporal mid-periphery, clinically consistent with an uveal melanoma.
Results: Enucleation was performed and histology revealed a well circumscribed and richly vascularized neoplasia in the anterior choroid, composed of cells with small round nuclei and eosinophilic fibrillar cytoplasm. Immunohistochemistry was negative for neurofilament, S100, CD56 and CAM5.2, whereas caldesmon and desmin were strongly positive, unveiling a smooth muscle phenotype, compatible with the diagnosis of mesectodermic leiomyoma.
Conclusion: Mesectodermic leiomyoma is an extremely rare tumour, with only 19 cases found in our review. It has a female predominance, occurs mainly in the cilliary body and is clinically indistinguishable from melanoma, leading most patients to eye enucleation. Such procedure could probably be avoided in some cases if a correct diagnosis could be made prior to an agressive surgical management, since the prognosis is generally very good.

PS-11-008
Prognostic role of chemokine receptor expression in conjunctival melanocytic lesions
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Objective: Chemokines have been shown to play a role in the progression and metastastic spread of uveal melanomas. The aim of this study is to examine the prognostic value of expression of chemokine receptors CCR7, CXCR4 and CCR10 in conjunctival melanocytic lesions.
Method: We examined the nuclear and cytoplasmatic expression of CCR7, CXCR4 and CCR10 in 39 nevi, 37 primary acquired melanosis (PAM) with and without atypia and 36 melanoma, by determining the immunoreactive score (IRS), using immunohistochemistry. The findings were correlated with progression of disease.
Results: A nuclear IRS <8 in CCR7 is seen in lesions with benign behaviour; a more benign course is also found in lesions with a low nuclear IRS in CXCR4, whereas an IRS >9 is only seen in PAM with atypia with malignant progression. CCR10 seems to be associated with an opposite behaviour, with a higher IRS concerning the nucleus being seen more often in lesions with a benign outcome. A high IRS concerning the cytoplasma is found in lesions with more aggressive behaviour, as is seen for CXCR4 and CCR10.
Conclusion: Chemokines seem to have prognostic value for patients with conjunctival melanomas and are associated with progression of PAM with atypia.

PS-11-009
A case of conjunctival myxoma in a child: A rare localisation
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Objective: Myxomas are benign neoplasms of mesenchymal origin that occur in the heart, and other organs but very rarely in the eye. Conjunctival myxomas classically present as slow-growing, painless, well-circumscribed masses. We reported this case because of the rarity of these tumours in conjunctival localisation and to point to differential diagnosis.
Method: The lesion was excised under local anaesthesia and reported to be a conjunctival myxoma. Clinical history, macroscopic, microscopic, histochemical and immunohistochemical analysis were used for differential diagnosis.
Results: A 11-year-old Turkish male with no history of ocular trauma presented with ocular pain, swelling, decrement in ocular vision in the right eye. The lesion was slow-growing, yellow-pink, translucent, solid well-circumscribed located in the temporal bulbar conjunctiva of the right eye. There were no systemic features, or family history of genetic conditions. The extirpated tumour, 13x10x3mm, was hypocellular and composed of spindle-shaped or stellate tumour cells. The tumour stroma showed extensive myxomatous changes.
Conclusion: The incidence of conjunctival myxoma is 0.001–0.002 % among conjunctival lesions. The mean age of the reported cases is

50 years (range, 18–80 years), with no gender predilection. The differential diagnosis of conjunctival myxoma includes amelanotic melanoma, fibrous histocytoma, lymphangioma, amelanotic nevus, lymphoma, myxoid neurofibroma, spindle cell lymphoma or rhabdomyosarcoma. Conjunctival myxoma can be misdiagnosed as a conjunctival cyst. Conjunctival myxomas can occur in association with the Carney Complex, which is an autosomal dominant syndrome associated with benign tumours, spotty mucocutaneous pigmentation, and endocrine overactivity.

PS-11-011

Orbital cystic schwannoma arising from optic nerve

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Objective: Most of the primary tumours of optic nerve are meningiomas and gliomas. Schwannomas arising from optic nerve are extremely rare lesions and only a few case has been reported until today. These lesions are slow-growing, well-circumscribed, solid/cystic masses. Here we reported a rare lesion schwannoma located in optic nerve with a cystic morphology.
Method: case report
Results: A 57-year-old female patient presented with a left ocular pain and progressive left proptosis. The patient was otherwise healthy. Orbital magnetic resonance imaging revealed an intraconal heterogeneous mass of 25 mm × 18 mm, radiographically consistent with a cavernous hemangioma. Surgical resection was performed and according to histopathological and immunohistochemical examination the final diagnosis was determined as "Orbital Schwannoma with Cystic Morphology".
Conclusion: Peripheral nerve tumours comprises 2 % of all orbital tumours and schwannomas are the most common types. Schwannomas are benign tumours arising from Schwann cells and most commonly involve trigeminal nerve root in intracranial location. Even if it is rare, schwannomas arising from optic nerve can be seen and cystic morphology of these tumours should not mislead the diagnosis.

PS-11-012

Keratoplasty in patients with Acanthamoeba keratitis: A study of three cases

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Objective: Corneal infections by amoebas present difficulties for clinical diagnosis and may be confused with other keratitis of the herpetic, fungal or bacterial type. We reviewed the clinical features and evolution in three patients with amoebic keratitis who required corneal transplantation after failure of medical treatment.
Method: The studied samples were three specimens of penetrating keratoplasty. Patients were two women aged 22 and 28 years and a 40- year-old male. One patient underwent a small corneal biopsy 1 week before transplantation, which was negative for amoebae. Samples were processed in a conventional manner and in addition to H/E sections Trichrome, PAS and Gram techniques were performed.
Results: The three patients revealed corneal cysts and trophozoites of Acanthamoeba. The epithelium was detached in all three although only two presented significant ulceration. One of the patients who had developed a crystalline keratopathy had superficial stromal band deposits interpreted by accumulation of the drugs used in their treatment.
Conclusion: The difficulty of reaching a clinical diagnosis of certainty is reflected in the negativity of cultures in all three patients although all had a history of contact lens use. For this reason they had received combined antibacterial and ant-amoebic treatment and one of them antifungal.

PS-11-013

New diagnostic approaches to uveal melanoma: EGFR, TGFb and MMP9 expression correlate with histological type and invasiveness

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Objective: The purpose of the present study was to investigate the relationship between MMP9 expression and scleral invasion of uveal melanoma (UM). We also examined the effect of growth factors (TGFb and EGF), oncosuppressor protein (p16) on the histological types and mitotic activity of tumour.
Method: Tumour specimens were obtained from 42 primary UM immediately after enucleation.
Results: Hyperexpression of MMP9 and EGFR were correlated with a high proportion of spindle cells in UM (Kruskal-Wallis test $p < 0{,}05$ for each). Moreover, we have demonstrated the association between the level of EGFR, TGFb and MMP9 expression to the initial stage of tumour invasion (Spearman's test $p < 0{,}05$). Moreover, there was a correlation between TGFb hyperexpression and mitotic activity (Spearman's test $p = 0{,}059$). Furthermore, a low level of p16 expression in UM was proportional hyperexpression of TGFb.
Conclusion: EGFR and MMP9 are known to be used as targets for anticancer therapy. The results of our study are suggesting to develop newer approaches of UM treatment on the early stages of invasion in order to keep an affected eye as an organ. Thereupon, it was concluded about the key-role of abnormalities in TGFb-pathway that cause the down-regulation of p16-gene, where the latter may lead to increased mitotic rate.

Tuesday, 5 September 2017, 09:30–10:30, Hall 3
PS-12 Cardiovascular Pathology

PS-12-001

Skeletal muscle biopsy in the diagnostic algorithm of rare cardiomyopathies - a retrospective study

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Objective: To highlight the usefulness of performing skeletal muscle biopsies in the work-up of cardiomyopathies with skeletal muscle involvement. Cardiac abnormalities are common during the evolution of many neuromuscular diseases, manifesting as dilated or hypertrophic cardiomyopathies, arrhythmias or conduction disturbances. While in most cases the onset is late, the cardiac symptoms may dominate the clinical picture or even precede the myopathic signs.
Method: We retrospectively reviewed 463 consecutive muscle biopsies performed and analyzed in a 3 years period (2014–2016), using the Colentina Clinical Hospital Pathology Department database.
Results: The skeletal muscle tissue was obtained using open biopsy under local anesthesia; muscle cryosections served for histological, histoenzimological, immunohistochemical stains and complementary techniques of western blotting and electron microscopy. We diagnosed two cases of desmin-related myofibrillar myopathies, one later proved to be caused by a newly identified form of mutation in desmin, the other carrying an additional mutation in alpha-B crystalline gene, two cases of acid maltase deficiency with cardiac involvement, one case of Danon disease, a multi-minicore myopathy with cardiomyopathy and one gamma sarcoglycanopathy with severe cardiac signs.
Conclusion: The morphological aspects enabled us to establish the diagnosis with major impact on clinical management and directed further confirmatory genetic testing.

PS-12-002

Biomechanical properties studying of atherosclerotic aortic wall with micro and macrocalcifications

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Objective: In the aortic wall calcification occurs as a pattern of micro and macrocalcification changing significantly aortic wall biomechanical properties. The aim of the work is biomechanical properties studying of aortic wall in the conditions of macro and microcalcification.
Method: 18 atherosclerotic aorta tissue samples with histologically verified different calcification patterns were studied. The samples were divided into 3 groups: control - without calcification manifistation (6), with microcalcification - calcium deposits to 4.99 mm (6), macrocalcification - calcifications <5 mm (6). Hydrostatic test stand was to study tissue samples strength, using the principle of equal distribution of pressure and its gradual increase on the sample surface. The experimental stand consists of metal container, filled with liquid under pressure of 5–8 bar, pressure conduit, a regulating valve, model manometer (accuracy class 0.4) and test chamber with fastening mechanisms of aorta samples. Moments of aortic wall rupture and the manometer index were fixed on the camera.
Results: For the control group pressure of aorta wall rupture was 389,19 ± 60,11 kPa. For aorta with microcalcifications rupture pressure was 128,63 ± 25,34 kPa, at the same time, the aorta with macrocalcification patterns rupture pressure was 344,0 ± 35,88 kPa.
Conclusion: Aorta samples with macrocalcifications are significantly more stable to hydrodynamic pressure, than aorta with microcalcifications ($p < 0.01$). Moreover, the resistance to pressure in the case of macrocalcifications is not significantly different from the control group ($p > 0.05$).

PS-12-003

Histopathologic patterns of pericardial and pleural metastases and their clinicopathological correlations

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Objective: The aim is to compare the histopathologic patterns of metastases involving pleural and pericardial tissues
Method: 145 specimens (75 pericardial and 70 pleural biopsies) were analyzed for the following patterns: (a) tumour cells floating into cavity without invasion of underlying tissue, (b) emboli, without invasion of underlying tissue or (c) invasive pattern, defined as neoplastic cells infiltrating into underlying tissue
Results: The invasive pattern of metastasis was mostly observed in pleural tissues (95, 7 %), whereas most pericardial metastases presented as tumour cells floating in the cavity or as lymphatic emboli (58, 6 %, $p < 0.0001$). The pattern of metastasis showed no correlation with the time to metastasis, the origin or the histologic type of the primary tumour. Breast cancer gave metastases more often in pleura, than in pericardium ($p < 0.0001$). Time to metastasis differed significantly ($p = 0.02$) in pleural (median 26.6 months) and pericardial (76 months) metastases as well as in comparison with primary tumour's origin ($p < 0.005$), as lung tumour gave metastases after 8.6 months, whereas breast tumour after 108.3 months.
Conclusion: Pericardial metastases in comparison to pleural ones present more often with floating tumour cells or emboli rather than invasive foci, a feature not associated with other clinicohistological characteristics, indicating an organ (pleura -pericardium) specific feature.

PS-12-004

Infarct-like medial necrosis: A role for ischemia in ascending aorta aneurysms

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Objective: The aim of this study is to evaluate the incidence and the relationship with other conditions of medial cell band-like necrosis resembling infarct—which appears in dissections and is considered a consequence of the cleavage - in ascending aorta aneurysms (AscAA), without cleavage.
Method: Slides and clinical files of 275 surgical specimens of patients with AscAA without dissection or previous aortic surgery were reviewed. Groups with or without infarct-like necrosis were compared by chi-square or t test; significance was established as $P \leq 0.05$.
Results: There were 47 cases with infarct-like necrosis. The variables with significant differences were: age (66.5 years in patients with vs 57.4 years in patients without infarct-like necrosis), atherosclerosis (53.2 % vs 28.9 %), inflammation (61.7 % vs 34.6 %), vasa vasorum alterations (66.0 % vs 50.0 %), systemic arterial hypertension (SAH - 85.1 % vs 68.4 %), and chronic renal dysfunction (19.1 % vs 7.5 %). No significant difference was detected regarding sex, adventitial fibrosis, Marfan syndrome, bicuspid aortic valve, smoking habit, diabetes, dyslipemia, ischemic heart disease, hypothyroidism, valve dysfunction, and sorological tests for syphilis.
Conclusion: Ischemic infarct-like necrosis is found in 17.0 % of cases of AscAA, and may play a role in its pathogenesis. It is related to SAH, chronic renal failure, atherosclerosis and signs of inflammation.

PS-12-005

Lymphangiogenesis is increased in aortitis and may reveal susceptibility for dissection

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Objective: Inflammation-associated lymphangiogenesis (IAL) is associated with various inflammatory states prone for rupture. The outer layer of the aortic wall is susceptible for dissection. Sparse data exist on lymphatics during aortitis and other aorta pathologies. The aim of the study was to delineate whether IAL impacts on the ascending aorta during inflammation.
Method: Surgically resected ascending aortas including 8 aortitis, 6 dissection, 7 atherosclerotic aortas, 5 severe degeneration without dissection and 4 autopsy controls were investigated. Lymphatics were detected by podoplanin antibody immunohistochemistry and morphometric analysis was performed with aim to evaluate both lymphatic density and lymphatic mean diameter.
Results: The lymphatic density of aortitis was increased ($p = 0.037$) as compared with dissection, atherosclerotic aortas, severe degeneration and autopsy controls.
Conclusion: Inflammation-associated lymphangiogenesis is increased in aortitis as compared with aortas without inflammation. The locality of IAL may predict susceptibility for dissection.

PS-12-006

The diagnostic efficacy of cardiac scintigraphy with 99mTc-labeled pyrophosphate for identifying cardiac transthyretin-related amyloidosis: The comparative clinico-morphological study of heart

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Objective: to demonstrate of the diagnostic efficacy of cardiac scintigraphy with 99mTc-labeled pyrophosphate (99mTc-PYP) for identifying cardiac transthyretin-related amyloidosis (ATTR).

Method: 61-year-old patient complained on the exertional dyspnea and was admitted to the clinic. Lower extremity edema, decreasing exercise tolerance appeared 3 years ago. History of hypertension and aortic stenosis made it difficult to carry out differential diagnosis of accumulation disease. Patient underwent echocardiography, single-photon emission computed tomography (SPECT) with 99mTc- PYP, endomyocardial biopsy and genetic analysis. We used Congo red staining, polarization and immunohistochemistry.
Results: Transthoracic echocardiogram revealed restrictive diastolic dysfunction of both ventricles. Ejection fraction (30 %) and global longitudinal strain (2–3 %) were reduced. SPECT showed the high accumulation level of 99mTc- PYP in the myocardium of left and right ventricles. The heart-to-contralateral ratio was 2,66. The amyloid deposits were located in myocardial interstitium as well as in the wall of small vessels. Immunohistochemical analysis revealed the expression of transthyretin in the areas of amyloid deposition. Genetic research was done by Sanger's sequencing method. The replacement Phe53Leu in the TTR gene was found and concluded as hereditary ATTR.
Conclusion: 99mTc-labeled pyrophosphate scintigraphy is an effective non-invasive diagnostic method that allows to identify cardiac ATTR.

PS-12-008
Morrow's myectomy
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Objective: Septal sub-aortic myectomy, invented by Andrew Glenn Morrow, was first used to treat left ventricle outflow-tract obstruction in Hypertrofic Cardiomyopathy and afterwards extended to other prominent ventricular hypertrophies and septal angulation. The authors intend to present the histomorphological pattern of a series.
Method: Retrospective study of patients submitted to surgical septal sub-aortic myectomy (June 2007-July 2016), due to septal hypertrophy. Demographic, clinical, echocardiographic and anatomo-pathological data was evaluated.
Results: 56 patients, 37 (66.1 %) females, median age = 67.5 year-old, 26 (46.4 %) due to calcifyed degenerative aortic valve, 25 (44.6 %) with hypertension history, 30 (55.6 %) due to symptomatic isolated obstructive septal hypertrophy. According to clinical and echocardiographic criteria, 25 patients (44.6 %) had obstructive hypertrophic cardiomyopathy phenotype. All patients with aortic valvular stenosis were submitted to prothesis implantation and myectomy, 12 patients (21.4 %) to isolated myectomy and the other (32.2 %) to myectomy and a mitral valve apparatus surgical procedure. The final anatomo-pathological diagnosis was hypertrophy in 52 cases (92.9 %), aortic sub-valvular membrane (stenosis) in 2 (3.6 %) and hypertrophic cardiomyopathy in 2 (3.6 %).
Conclusion: Morrow's Myectomy relevance relies on the diagnosis, with anatomo-pathological characterization of surgical specimens' microscopic features, as well as on patients' daily life improvement and prevention of many sudden cardiac deaths.

PS-12-009
Cardiac Myxoma: Review of clinical and histopathological features of 8 cases at Hospitalary Complex of Navarra
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Objective: Myxoma is the most common primary tumour of heart, although still rare. These tumour are benign but malignant in a sense that often embolizes and may cause severe complications. We report our experience with cadiac myxoma in adults at Hospitalary Complex of Navarra.

Method: Eight patients resected for primary cardiac tumours between Jan. 2007 and Jan 2017 . We retrospectively reviewed their clinical, immunohistochemical and pathological findings.
Results: The mean age at the time of resection was 50.37 years (range 21–73). All the patients were females and one case was disgnosed during pregnancy. The most common clinical presentation was arterial embolisms (80 %). Most common location was left atrium. Mean size were 24.85 mm. Multiple myxomas were found in two out of eight patients reviewed and both tumour had recurrence 2 years after resection. All the tumours had characteristic stellate cells in a myxoid background, and 25 % showed ossification, 37.5 % Extramedullary haematopoiesis, glandular structures (12,5 %) and granulomas (12,5 %). All cases revealed strongly positive vimentin and CD34.
Conclusion: Cardiac myxoma is more common in young women. Although cardiac myxoma is a benign tumour, embolisms may cause severe complications. A better understanding of the histopathologic features of cardiac myxomas would facilitate the proper management and improve prognosis.

PS-12-011
Lack of expression of ascending aortic wall estrogen receptor beta - a potential clue for aortic valve stenosis?
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Objective: Aortic valve stenosis may be associated with post-stenotic dilatation of the stiff-walled atherosclerotic ascending aorta, which is seldom at risk for dissection. Aortic wall estrogen receptor beta (ER) positivity may protect from atherosclerosis of the dilated ascending aorta. We studied the presence of aortic valve stenosis during dilatation of the ascending aorta in respect to aortic wall ER positivity.
Method: Aortic wall histology (Elastase, HE, AbPAS staining) and immunohistochemistry for ER, T/ B-lymphocytes, plasma cells, macrophages, endothelial cells, smooth muscle cells, and cell proliferation, were performed in 30 patients that underwent surgery for the ascending aorta, and the samples were grouped according to presence of ER positivity.
Results: 23 patients were operated due to dilated ascending aorta and 7 due to dissection. Two patients with ER had aortic valve stenosis, in contrast to eight without ER. Macrophages of the media were increased in patients with ER as compared to those without ER (1.75 ± 0.28 vs 1.08 ± 0.17, $p = 0.044$, respectively). Receiver operating characteristic curve (ROC) analysis showed that dilated ascending aorta with medial ER is seldom associated with aortic valve stenosis (AUC 0.805; SE 0.081; $p = 0.008$; 95 % CI 0.646–0.964). Aortic wall medial ER is inversely correlated with the severity of aortic valve stenosis (R2 linear = 0.937, $p = 0.009$).
Conclusion: Lack of dilated ascending aortic wall ER is associated with aortic valve stenosis reflecting atherosclerosis and stiffness of the ascending aorta resisting dissection. Positive ER immunohistochemistry may guide the surgeon to consider the radical resection of dilated ascending aorta.

PS-12-012
Immunohistochemical characteristics of aortic valve in the case of atherocalcinosis
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Objective: According to the results of the Euro-Heart Survey on Vascular Heart Disease the most common pathology is nonrheumatic aortic stenosis, it is also called as calcific aortic valve stenosis (CAVS), as in its pathogenesis the process of biomineralization of valve cusps and ring plays the main role.

Method: 30 samples of mineralized aortic valves (I group) and 10 samples of aortic valve without evidence of biomineralization (II group - control) were studied. Immunohistochemical study of expression of collagen I, CD68, MPO, S100A9), caspase 3 and osteopontin was conducted in AV tissue of both groups.
Results: In CAV tissues the fibrillar component (collagen I) growths was found, but the quantitative compositions of circulating inflammatory cells (CD68+) are not significantly different from the control group. CAVs contain much more MPO+ -cells ($p < 0.001$) in comparison to the group of AV without biomineralization. Our data show a significant increase of the S100A9 and OPN expression in the mineralized tissue of AVs ($p < 0.01$). Also a higher expression level of Casp3 and MPO was found in CAVs ($p < 0.05$).
Conclusion: High Casp 3 expression confirms the increased level of cell elimination in the CAVs tissue, which is obviously connected with the impact of high local concentrations of S100A9. These facts can contribute to the development of pathological biomineralization of AV. Since osteopontin inhibits the hydroxyapatite formation by binding to the surface of the crystals, its hyperproduction is a counteracting factor against biomineralization in AV tissue.

PS-12-013
Post-mortem pathological investigation of early myocardial damage: A review of fluorescent markers and immunohistochemical procedures
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Objective: Post-mortem diagnosis of early ischemic lesions of the myocardium is a key issue in forensic pathology. This study present the prominent histochemical and immunohistochemical methods and analyse their diagnostic accuracy and the potential timeframe of their use.
Method: An extensive literature review has been conducted using electronic databases of peer-reviewed international journals, textbooks and guidelines. We emphasized in the selection of comparative studies between various markers from cases with varying post-ischemia intervals to facilitate the differential analysis of their distribution patterns and the temporal evolution of their biological substrates and therefore signal.
Results: Acridine-orange and hematoxylin-eosin autofluorescence are the main fluorescent markers in use, with the former showing satisfactory sensitivity and specificity after 2 h of ischemia. The immunohistochemical detection of cellular proteins depletion [H-FABP, desmin, myoglobin, troponin C and T] was found to begin early and correlate with the ischemic process well. On the other hand, fibronectin and fibrinogen deposition requires a longer postischemic period and yields spatially different results. Finally, the visualization of the C5b-9 complement complex on and in myocytes sets in 30–40 min after the onset of ischemia.
Conclusion: The integrated combination of these markers combined with the research on fast post-mortem analysis of cryosectioned tissue should improve our diagnostic potential.

PS-12-014
Evaluate fibrous loosening of cardiovascular tissues due to ageing
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Objective: Due to fibrous loosening by ageing, aortic dissection, valvular regurgitation, and cord rupture of mitral valve occur. We have tried to evaluate degree of loosening by the values of speeds-of-sound(SOS) which has strong correlation with tissue stiffness. Do SOS through tissues correspond to tissue loosening? Which chemical changes happen at the site of loosening?
Method: We compared the SOS images between lesions and normal areas. To investigate the sensitivity to protease digestion, we compared the SOS images before and after digestion. To detect chemical changes of the tissues, lysyl oxidase (LOX), fibronectin (FN), and vitronectin (VN) were stained by specific antibodies.
Results: The lesions of aortic dissection, valvular regurgitation, and cord rupture of mitral valve showed slower SOS than the surrounding normal areas and were vulnerable to protease digestion. LOS stainings were weak and FN and VN stainings were stronger compared with the surrounding tissues.
Conclusion: The degree of fibrous loosenings corresponded well to the reduced values of SOS. In chemical alteration, cross-linking between collagen fibers decreased and matrix proteins such as FN and VN increased in amount.

PS-12-015
A rare case of primary cardiac osteosarcoma: The importance of the pathological diagnosis
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Objective: Most tumours arising from the heart are benign and when malignant, they tend to be metastatic. Primary cardiac osteosarcoma is a very rare entity which accounts for less than 10 % of primary malignant heart tumours and is generally located at the left atrium.
Method: A 70-year-old female patient presented with a nodular mass of the left atrium, clinically resembling myxoma. No past medical history or further symptoms were mentioned. The mass was excised and pathological examination followed.
Results: Sections showed a spindle cell neoplasm with a fascicular architecture and moderate or high cellularity. The neoplastic cells were highly pleomorphic and atypical. Abundant mitoses were found. Tumour cells produced large amounts of osteoid matrix. Chondroid differentiation was evident, as well. Immunohistochemical panel, including vimentin, AE1/AE3, CK8/18, EMA, CD99, CD31, calretinin, SMA, desmin, S100 and CD34 revealed vimentin positivity of the neoplastic cells. Bone scan and thoracic-abdominal computed tomography were followed, which did not show any signs of distant metastasis or another primary tumour. Nine months later, the patient is free of disease.
Conclusion: The pathological diagnosis of primary cardiac osteosarcoma is of great importance for the patient, because it is usually misdiagnosed as myxoma clinically.

PS-12-016
The influence of clinical determinants on aortic diameters - an autopsy morphometric study
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Objective: The authors compared aortic diameters in relation with patients' gender and age.
Method: The studied material consisted of aortic cross sections at four different levels (the ascending aorta—AscAo, the aortic arch—AoArch, the distal thoracic aorta—DTAo and the abdominal aorta—AbdAo) fixed in buffered formalin from 91 patients deceased during hospitalization and autopsied. The mean diameter of each section was determined with specially designed image analysis software.
Results: The men had larger mean dimeters than women in all four sections. All assessed aortic mean diameters were increasing with age. AscAo diameter had the most obvious increasing, while AbdAo diameter had a mild progression with age.
Conclusion: Aortic dimensions undergo a remodeling process influenced by gender and the ageing process. There was no other autopsy study to present reference values of the aortic segments diameters therefore further studies on larger series are required to validate these observations.

Tuesday, 5 September 2017, 09:30–10:30, Hall 3
PS-13 Digestive Diseases Pathology - GI

PS-13-001
Gastric carcinoma with lymphoid stroma: Analysis of microsatellite instability and Epstein-Barr virus status
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Objective: Analyze microsatellite instability (MSI) and Epstein-Barr virus (EBV) status in gastric carcinoma with lymphoid stroma (GCLS), and characterize its clinicopathological features.
Method: GCLS cases were retrieved from the archives and reviewed by an experienced dedicated gastrointestinal pathologist. Expression of EBV encoded small RNA (EBER) by in situ hybridization and MSI status were assessed in 18 cases of GCLS diagnosed between 2000 and 2017. MSI status was evaluated by MLH1, MSH2, MSH6 and PMS-2 immunoexpression. Relevant clinical data was collected from patients' charts.
Results: GCLS was more prevalent in men (61.1 %) and in proximal lesser gastric curvature (55.5 %) with a mean age of 60.7 years. During follow-up one patient presented metastasis and died from disease. Diffuse positivity for EBV hybridization was observed in 13 (72.2 %) GCLS, whereas weak and focal positivity was detected in 3 (16.6 %) cases. Loss of MLH1 and PMS2, indicating altered expression of MLH1, was found in 2 (11.1 %) cases, one of them with simultaneous weak and focal EBER expression.
Conclusion: The global characteristics of this series are in accordance with previous publications. Although EBV infection and MSI, considered the two main carcinogenic pathways involved in GCLS, have been considered mutually exclusive, our results suggest that some cases might share both features.

PS-13-002
Histopathological evaluation of gastric polypoid lesions: A single institutional study
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Objective: To identify the prevalance and characteristics of the gastric polypoid lesions detected by endoscopy.
Method: The records of 45270 patients who underwent endoscopy between January 2007 and March 2017 were reviewed retrospectively. The patients with gastric polypoid lesions were evaluated in terms of age, gender, histopathological diagnosis and anatomical location.
Results: A total of 996 (%2.2) patients were found to have at least one polypoid lesion whereas 214 patients had 2 or more. Of all 1209 lesions, 19.2 % were neoplastic and 80.8 % were non-neoplastic lesions. Hyperplastic polyp was the most common (58.6 %) followed by foveolar hyperplasia (17.4 %), fundic gland polyp (11.5 %) and well-differentiated neuroendocrine tumour (4.7 %). Adenomatous and inflammatory fibroid polyps (2.2 %) were less common. H.pylori incidence in hyperplastic polyps was 27.7 %. The most common anatomical location was the antrum (42.5 %). The mean age was 60.3 and female to male ratio was 1.59. Focal dysplastic changes were seen in 1.6 % of hyperplastic polyps and 0.5 % showed adenocarcinoma within the polyp.
Conclusion: Gastric polypoid lesions are common endoscopical findings and histopathological diagnosis should be made carefully since there is a variety of lesions that can present as polyps. The dysplastic changes and malignant transformation in hyperplastic and adenomatous polyps should be kept in mind.

PS-13-003
Endoscopical submucosal dissection of leiomyomas in the oesophagus: 7 cases
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Objective: Endoscopical submucosal dissection (ESD) is being used more frequently in recent years for en bloc resection of large gastric and colonic tumours and now for the removal of esophageal tumours. Here, we report a case series of esophagial tumours resected by ESD all of which were diagnosed as leiomyomas.
Method: The records of patients who underwent ESD for esophagial lesions between 2014 and 2016 were retrieved and seven cases of esophagial smooth muscle tumours were found. The cases were then evaluated depending on gender, localisation, size and immunohistochemical profile.
Results: Five of the patients were female whereas 2 were male. The median age was 58 years (range 39–62 years). The locations of all tumours were in the lower 1/3 portion of the oesophagus. The largest tumour had a diameter of 4.5 cm, the mean tumour size was 2.7 cm and the cut surface was solid and grey in all. Microscopically, the tumours were made of fascicles of spindle cells with no atypia and mitosis. Immunohistochemical studies showed diffuse positivity for smooth muscle actin and desmin and negativity for CD117 and CD34 in all of the cases. Six of the cases were negative for S-100 protein whereas one case showed focal weak positivity. The Ki-67 index was <1 % and complete resection was achieved in all of the tumours.
Conclusion: ESD is a safe and effective procedure for treating esophageal tumours and complete resection is possible in experienced hands.

PS-13-004
Study of a metastatic colon cancer model to the liver: Clinicopathological results
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Objective: This study aimed to analyze clinicopathological features of 57 patients that developed adenocarcinomas in the colon with progression to liver metastasis.
Method: Fifty-seven colon adenocarcinomas (CA) and their respective hepatic metastatic adenocarcinomas (MA) were microscopically examined. Diverse histological parameters such us necrosis, mitotic activity, grade of differentiation, inflammation, tumour buds… were analyzed. Clinical data such as survival rates and demographic parameters were also recollected.
Results: Our database is composed of 38 men and 19 women with a mean age of 66.2 ± 9.6 years. About 79 % of cases were from the left colon. Histopathologically, almost 89 % CA presented tumour buds and almost 52 % showed metastatic regional lymph nodes on diagnosis. The tumoural grade was higher in CA (1.8/3 in CA vs 1.6/3 in MA); mitotic activity per 10HPF was almost equal (35 ± 22 in CA vs 34 ± 20 in MA); intratumoural necrosis was significantly higher in MA (3.6/4 in MA vs 2.0/4 in CA). Minimal differences were observed concerning peritumoural chronic inflammation (1.3/4 in CA vs 1.2/4 in MA) . Statisticlally, presence of tumour buds in CA correlated with lower progression-free survival ($p = 0.013$).
Conclusion: We have described relevant histopathological differences between CA and MA. Tumour buds in CA correlated with lower progression-time survival.

PS-13-005

Gastric carcinoma with lymphoid stroma: Clinicopathologic study of 5 cases

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Objective: Gastric carcinoma with lymphoid stroma (GCLS) is a rare and distinct subtype of gastric cancer associated with better prognosis than other types of gastric carcinoma and may be associated with latent Epstein-Barr virus (EBV) infection or microsatellite instability.
Method: The aim of this study is to characterize the clinicopathologic, histologic features and immunohistochemical results of five cases diagnosed from 2011 to 2016 at our institution.
Results: The mean age of the patients was 59.4 years (40–78), one female and four males. 60 % were found at cardia and their size ranged from 26 to 155 mm (mean 70.8). Microscopically, all tumours were composed of poorly differentiated epithelial cells surrounded by lymphocytic infiltration. Only one tumour was PD-L1 positive. None of the tumours were positive for Epstein-Barr virus. The staging on diagnosis was pT2-1, pT3-2, pT4-2 and 4 had lymph node metastasis. One patient had neither chemo nor radiotherapy. The mean follow-up is 32.6 months (range 12–68). All patients are alive and well with no signs of disease recurrence.
Conclusion: This group of patients had high stage but are all alive and well. GCLS represents a distinct morphological subtype and has an excellent prognosis compared with the more common gastric adenocarcinomas.

PS-13-006

Unexpected histopathologic findings in cholecystectomy specimens

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Objective: Pathologic evaluation of the gallbladder after cholecystectomy is a routine practice. On occasion, it can lead to unexpected but significant pathologic findings. The aim of this study was to determine the prevalence and types of pathologic diagnoses found in routine cholecystectomy specimens at our institution.
Method: Cholecystectomy specimens submitted for pathologic evaluation (between 2014 to 2016) were retrospectively reviewed and pathologic diagnoses were recorded.
Results: 1254 gallbladder specimens were identified. Histological examination of the surgical specimen revealed chronic cholecystitis in 75.6 % (n = 948), acute cholecystitis in 14.7 % (n = 184), cholesterol polyp in 5.6 % (n = 70) and metaplasia in 2.9 % (n = 37). Neoplastic, pre-malignant or malignant diagnoses were noted in 1,2 % (n = 15) of specimens. These included: adenomas (n = 4), BilIN (n = 4), adenocarcinoma (n = 5), metastatic adenocarcinoma (n = 1) and primary Hodgkin lymphoma (n = 1).
Conclusion: Our data revealed a large array of findings in routine cholecystectomy specimens, which included inflammatory conditions, and various benign as well as malignant neoplasms. This study highlights the importance of sampling and microscopic examination of all specimens to identify unsuspected conditions, which may require further postoperative management.

PS-13-007

Importance of endoscopic biopsy of the ampullary region: Diagnostic value, concordans and related parameters

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Objective: Endoscopically suspicious papillae are often biopsied to assess malignancy and to establish treatment strategies. We aimed to evaluate the diagnostic value of endoscopic ampullary biopsies and to reveal the concordans with resections.
Method: A total of 188 ampullary biopsies and 40 follow-up resections were evaluated (2010–2017). Demographic data of patients, endoscopic appearance of the papillae, size and number of biopsy specimens and diagnoses were noted.
Results: F/M was 1,1 (100/88) and the mean age was 62(22–91). Of 188 biopsies; 102 diagnosed as acute/chronic inflammation, 27 adenomatous changes with low or high grade dysplasia , 34 adenocarcinoma and 25 other. Six cases (%15) were rebiopsied multipl times. The overall accuracy was 82 % (n = 34) between biopsies and resections. Cases with no correlation (n = 6) were reviewed and the reasons for underdiagnosis was established as; crush artefact in 3 % (n = 1), superficial or inadequate sampling in 97 % (n = 5).
Conclusion: Ampullary carcinomas have better prognosis than pancreatic ductal carcinomas. Endoscopic biopsies seem to be an appropriate way to diagnose ampullary malignancies and to decide their treatment . Unsatisfactory material is the main reason for multiple biopsies, and delayed diagnosis. Recuts , P53 and Ki67 are very helpful to evaluate the presence of invasive carcinoma.

PS-13-008

Trend of gastrointestinal lymphomas in North India: A 5 year study done in a tertiary health care institution

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Objective: The objective of the study was to classify and categorise various gastrointestinal lymphomas in Indian population.
Method: Descriptive Study of samples collected between July 2010 and Novembe3r 2016.
Results: During this period 3119 GI malignancies were diagnosed on GI biopsies of which, 101 (3.2 %) cases were gastrointestinal lymphomas including both primary and secondary types. The primary GI lymphomas were 1.1 % of total GI malignancies. The most common site for primary GI lymphoma was stomach (44.4 %), followed by small intestine and illeocaecal region (22.2 %). The most common primary lymphoma was diffuse large B cell lymphoma (36.1 %). The unusual lymphomas were 01 case of immunoproliferative small intestinal disease, 02 cases of anaplastic large cell lymphoma, 02 cases of gastric plasmablastic lymphoma, 01 case of denovo follicular lymphoma, 01 case of enteropathy-associated T-cell lymphoma, 02 cases of post-transplant lymphoproliferative disorder, 01 case of intestinal NK/T cell lymphoma and 01 case of gastric mantle cell lymphoma.
Conclusion: DLBCL constitutes the bulk of GI lymphomas in India as in other parts of the world with stomach being the most common site. Accurate diagnosis of the type of lymphoma is vitally important for correct treatment and determining prognosis.

PS-13-009

Loss of E-cadherin and B-catenin nuclear translocation in the invasion front is the central phenomenon of epithelial mesenchymal transition in colorectal cancer

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Objective: To investigate the epithelial mesenchymal transition (EMT) in colorectal cancer (CRC).

Method: In 50 consecutive cases of CRCs immunohistochemical stains were performed with E-cadherin, N-cadherin, β-catenin and SLUG. The expression of these antibodies was evaluated in the tumour core and tumour buds. The buds were classified from G1 to G3 based on the number of isolated cells in the invasion front.
Results: 12 cases were staged as pT1-2 N0, 26 as pT3N0 and 12 as pT3N1-2. The budding phenomenon was mostly high grade (G1-n = 12; G2-n = 28; G3-n = 10). SLUG positivity/ N-cadherin negativity was observed in 47/50 cases in both core and invasion front. E-cadherin showed diffuse positivity in core and buds in 21/50 cases. The other 29 cases were focally positive in the core (10 G3- and 19 with G2-buds). In the invasion front all of the 10 G3-cases, E-cadherin was lost and β-catenin membrane to nuclear switch was observed. The 21 cases with diffuse E-cadherin positivity also presented β-catenin membrane positivity.
Conclusion: In CRC, loss of E-cadherin and β-catenin nuclear translocation in the invasion front seems to be correlated with the tumour budding grade, as an indicator of tumour agressivity. This work was supported by the UMF Tirgu-Mures, Romania, project frame 275/11.01.2017.

PS-13-010
Mucinous neoplasms of the appendix: Some overlapping aspects with distinct outcomes
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Objective: The differentiation between low and high-grade in mucinous neoplasias is essential due to differences in behavior and management. Besides their innocuous appearance, low-grade appendiceal mucinous neoplasms (LAMN), can disseminate to the peritoneal cavity as pseudomyxoma peritonei and still have an excellent prognosis, challenging our definition of malignancy.
Method: A retrospective analysis on clinical data and histopathologic slides was performed on 32 mucinous neoplasms of the appendix, from 2001 to 2016.
Results: There were 23 LAMN: 5 males and 18 females, mean age 61 (21–85) and eight had extramural mucin. The mean follow-up was 56 months (5–138) and 17 are alive, 5 died from other causes and 1 was lost for follow-up. There were nine adenocarcinomas: 5 males and 4 females, mean age 55 (29–83), mean follow-up of 45 months (0–131). Stage pT1-1, pT2-2, pT3-2 and pT4-4, one had lymph node metastasis and another was M1. Five are alive and four died with disease.
Conclusion: No patient with LAMN had recurrence or died of disease. There were no differences in outcomes between presence of intra or extramural mucin. The differences in nomenclature for these lesions in the literature require more studies to define firm criteria for diagnosis, especially in 'borderline' lesions.

PS-13-011
Fluorimetry as a new approach to investigate colon cancer cancerogenesis
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Objective: To compare spectral properties of colonic adenomatous polyps depending on histologycal types and degree of dysplasia with each other and adenocarcinoma.
Method: Spectra of autofluorescence excitation from unstained histologycal sections were measured after devaxing on spectrofluorimeter SOLAR CM-2203. The wavelength of registration was 410 nm after its excitation in UV region. Basing on microscopical picture, colonobiopsies were divided into following groups: adenocarcinomas—11 cases, colonic adenomas (tubular – TA (41) and tubulo-villous – TVA (10) with high or low dysplasia and III and 13 cases of almost normal mucosa.
Results: Spectra of all types of lesions have two maxima at 265÷270 nm and 330÷340 nm. The first maximum is defined by tryptophan-containing peptides, the second maximum by collagen. Progression towards cancer leads to increase of NADH concentration impacting in the second maximum of spectra. Regardless to degree of dysplasia, spectra of TA are closer to spectrum of normal mucosa, and spectra of TVA are more similar to spectra of moderately differentiated adenocarcinoma (even then to well-differentiated adenocarcinoma).
Conclusion: This finding shows, that type of adenomatous polyp is more important for determination of malignization risk than degree of dysplasia.

PS-13-012
Different patterns of the prevalence and spatial distribution of intestinal metaplasia subtypes in gastric mucosa
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Objective: The objective of the current study was to analyse the prevalence of intestinal metaplasia subtypes and their spatial distribution.
Method: 1012 adult patients aged 40–64 years referred for upper endoscopy were enrolled into the study (GISTAR study in Latvia). Altogether, five biopsy samples from each patients were obtained from from the antrum, incisura angularis and from the corpus. The slides were stained with haematoxylin and eosin (H&E), alcian blue (AB) and high iron diamine alcian blue (HID-AB) when IM was observed by AB staining.
Results: IM was found in 231 subjects (22.08 %). The prevalence of the type I IM was 79.3 %, whereas the prevalence of of type II IM was 12.5 % and type III IM was 8.2 %. The distribution of type I IM in incisura angularis was significantly higher compared to antrum ($p < 0.05$). Furthermore, the distribution of type III IM was higher in antrum greater compared to antrum lesser curvature.
Conclusion: To conclude, the prevalence of biopsies carrying for complete IM was 79.3 %, whereas for incomplete IM was 20.7 %. Type I complete IM and type III incomplete IM was more frequently found in antrum compared to corpus.

PS-13-013
Plexiform fibromyxoma of the stomach: A rare diagnosis
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Objective: Plexiform fibromyxoma (PF) is a rare benign mesenchymal tumour, typical of the pyloric antrum or duodenal bulb. PF can be misdiagnosed as gastrointestinal stromal tumour (GIST), but the prognosis is good with little recurrence reported.
Method: We report cases from 2 patients, female aged 51 (case 1) and male aged 46 (case 2), who underwent subtotal gastrectomy.
Results: Macroscopically, both were multinodular and glistening, measuring 2.7 cm (case 1) and 5.5 cm (case 2) across. Both tumours were centered in the muscularis propria, dissecting muscle in a multinodular/plexiform growth pattern, focally reaching subserosa. They were composed of an arborizing capillary network and bland spindle cells which were separated by abundant myxomatous stroma, with nodules protruding downward within the subserosa and no mitotic figures. Immunohistochemical studies were negative for CD117, DOG1, CD34, S100, actin and desmin. The second case was focally positive for CD10.
Conclusion: Plexiform fibromyxoma, a rare tumour, may be misdiagnosed as inflammatory fibroid polyp or plexiform neurofibroma; however, the differential diagnosis with highest clinical impact is plexiform myxoid GIST, a potentially malignant neoplasm requiring follow-up.

PS-13-014

A new challenging pattern of gastrointestinal stromal tumour - insights from a case report

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Objective: Gastrointestinal stromal tumours (GISTs) are well known to have many different morphological patterns and this is even more prominent in post Imatinib treatment relapses. Some patterns could be challenging, as this case demonstrates.
Method: We report the case of a patient submitted to peritoneal implants resection and hepatic metastasectomy, after polar gastrectomy and Imatinib treatment for a gastric GIST and a partial nephrectomy for a kidney tumour.
Results: We received multiple peritoneal nodules and a liver metastasis from a 49 years-old man diagnosed with gastric GIST 5 years before. He completed 3 years of Imatinib, till he was submitted to a kidney tumour surgery. All nodules were morphologically similar (mixed pattern GIST with degenerative changes, positive for CD117 and DOG1), except 1, composed by epithelioid clear cells, negative for CD117, DOG1, citokeratines and PAX8. PCR analysis of this lesion allowed the detection of the same c-KIT gene mutation observed in the "classical nodules".
Conclusion: As far as we know, this is the first time that an after Imatinib epithelioid clear cell GIST pattern is described. This case is an example of a new diagnostic challenge to consider on the recognition of morphological patterns after therapy.

PS-13-015

Mismatch repair proteins and epithelial mesenchymal transition in colorectal cancer

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Objective: Mismatch repair (MMR) deficiency is present in ≈ 15 % of colorectal carcinoma (CRC) cases, including Lynch syndrome(LS)-related cancers (Whitehall et al.,2011; Berginc et al.,2009). In turn, a relationship between epithelial-mesenchymal transition (EMT) and LS has been demonstrated (Gu et al.,2014). Our aim was to investigate EMT-MMR protein association in consecutive CRCs.
Method: By immunohistochemistry, expression of MSH2, MSH6, PMS2, MLH1, CD44, E-cadherin was detected. Expression intensity EI was measured in a 0–3 scale (0, no expression; 1-weak, 2-moderate, 3-strong). The final score was expressed as a sum of EIs by extent (%).
Results: Evaluating retrospectively 124 consecutive CRCs, loss of MSH2, MSH6, PMS2, and MLH1 was found in 1;0;11 and 4 cases, respectively. The MMR protein expression was reclassified as low versus high using the median as cut-off: MSH2 1.39; MSH6 1.9; PMS2 1.8; MLH1 1.43. The overall expression of E-cadherin was 1.81[95 % confidence interval: 1.74–1.89], of CD44: 1.29[1.16–1.41]. T test showed statistically significant difference in E-cadherin level by MSH2 (low 1.72[1.61–1.82]; high 1.91[1.81–2.01]; $p = 0.01$) or PMS2 (low 1.71[1.60–1.82]; high 1.95[1.85–2.05]; $p < 0.01$). CD44 showed significant difference by PMS2 (low 1.43[1.24–1.62]; high 1.17[1.00–1.34]; $p = 0.04$).
Conclusion: In the study, significant, complex associations are shown between EMT and expression level of MMR proteins in consecutive CRC.

PS-13-016

Pathohistological changes of gastric mucosa in wistar rats after acute exposure to orally administrated acrylamide

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Objective: In 2002, acrylamide is discovered as toxic byproduct in foods rich in starch, which are prepared at high temperatures.
Method: Ours research was carried out 6 groups of 5 experimental animals (Wistar rats). Two control groups orally implicated distilled water. Two experimental groups orally administrated acrylamide in a daily dose of 25 mg/kg, and two dose of 50 mg/kg. Three groups were sacrificed after 24 h and three after 72 h; On histological gastric tissue material is applied qualitative and semi-quantitative histological analysis and stereological measurements of individual compartments of the stomach mucosis.
Results: In the stomach mucosis of Wistar rats is seen direct slight damage of the surface epithelium, accompanying mild inflammatory reaction, degranulation of mast cells and slight thinning of lamina muscularis mucosae. After toxic effect on epithelium starts reconstruction of the epithelium, which is confirmed by the presence of immature form of mucoproductive cells. Examined inflammatory, degenerative and regenerative parameters show a positive correlation with respect to dose and/or a time of exposition to acrylamide.
Conclusion: Understanding the effects of acrylamide on gastric mucosa lead to adequate prevention in diet habits and treatment in gastric diseases.

PS-13-017

Histopathologic variations in gastrointestinal neuroendocrine tumours

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Objective: Gastrointestinal neuroendocrine tumours (GI-NETs) are relatively rare entities, a genetically diverse group of malignancies that lacks universally accepted standards for assessing biologic behavior.
Method: We conducted a retrospective study including 27 consecutive cases of GI-NETs. Multiple histologic and demographic features were recorded and correlated with Ki67 index.
Results: Mean age at diagnosis was 63.5 years (31–84) and M/F ratio was 4/5. Thirteen cases (48.15 %) had gastric origin, eight (29.63 %) involved the small intestine and six (22.22 %) originated in the colon. The average mitotic index was 7 mitosis/10 HPF (0.45 mm) (ranging from 1 to 22 mitoses). The average Ki67 index was 27 % (ranging from 66 % in colonic NETs to 18 % in gastric NETs). Ki67 expression had extremely significant association with tumour histological grade ($r = 0.89$, $p = <0.0001$) and mitotic rate ($r = 0.79$, $p = <0.0001$). Also, the histological grade was found to be correlated with the location of the tumour, colonic lesions being mostly high grade ($r = 0.39$, $p = 0.036$). There was no correlation between age and mitotic rate or histological grade.
Conclusion: Ki67 index correlates well with tumour grade and mitotic index, thus being helpful in routine histopathology practice. Location correlates with histological grade of GI-NET, colonic lesions being predominantly high grade.

PS-13-018

Confocal laser-scanning microscopy and conventional light microscopy targeting morphological changes in colorectal lesions

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Objective: Histological examination of gastro-intestinal lesions is based on conventional hematoxylin-eosin light microscopic images of thin-slice specimens. A study of a non invasive method that may yield immediate microscopic images of untreated tissue was carried out: laser-scanning confocal microscopy has the ability to serially produce thin optical sections through thick specimens.

Method: The study materials consisted of fresh human colon tissue that includes lesions as hyperplastic polyps and adenomas in addition to normal mucosa and adenocarcinomas. The confocal method offers virtual histological images of the lesions that were correlated to the corresponding histological sections in order to provide a morphologic parallel and to highlight the advantages and disadvantages between those two methods.
Results: The nuclei were not visualized in normal mucosa or hyperplastic polyps. In adenomas with high-grade dysplasia and adenocarcinomas, nuclei were more often visible than in adenomas with low-grade dysplasia.
Conclusion: Our findings show the utility of confocal microscopy as a promising technique that accurately visualizes histology in fresh, unstained tissues, enhancing early detection of gastro-intestinal pathologies, including premalignant lesions.

PS-13-019
Why should pathologist always report glandular atrophy in helicobacter pylori gastritis?
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Objective: Gastric dysplasia is the last step in Helicobacter pylori (HP) induced carcinogenesis, after glandular atrophy (GA) and intestinal metaplasia (IM). This study evaluates the significance of GA and IM for patients' outcome.
Method: We designed a case-control study including endoscopic gastric biopsies from 72 patients with similar demographic data (two groups: 36 patients with gastritis and dysplasia and 36 patients with gastritis without dysplasia).
Results: HP infection rate was higher in patients with dysplasia (91 % vs 52 %; $p = 0.073$). GA and GA-IM association were more frequent in dysplasia group ($p = 0.034$, respectively $p = 0.038$). No significant correlation between IM and dysplasia were found. In patients with dysplasia, minimal GA was associated with a higher density of HP (33.33 % vs. 5.55 %), whereas severe GA was linked to low density HP (2.77 % vs. 30.00 %).
Conclusion: There is a strong connection between HP status and subsequent premalignant changes. GA is the most significant indicator of evolution towards intraepithelial and invasive malignancy, so it is mandatory to be always evaluated and reported, in order to conceive a special management plan for patients with persistent atrophy after HP gastritis.

PS-13-020
Usability of p53 for demonstrating synchronicity in multiple colorectal adenocarcinomas
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Objective: Some patients with colorectal cancer have more than one distinct site of carcinoma. Multiple tumours can be synchronous carcinomas or one primitive tumour and its metastasis. The aim of our study is to establish the usability of p53 staining pattern to discriminate these cases.
Method: We retrospectively evaluated 22 consecutive cases of tumours to investigate the method used to establish their synchronous character. Most patients had two lesions, but we also had patients with more tumours. Data regarding demography, histologic subtypes, presence of adenomas, immunophenotype and p53 status were evaluated.
Results: The most frequent association is between adenocarcinomas (82 %). Other are between adenocarcinoma and mucinous carcinoma (9 %). and adenocarcinoma and neuroendocrine carcinoma (9 %). In only 4 % of the cases, identification of morphologic dissimilar patterns at least one of which being an unusual subtype was used for the diagnosis. We established the diagnosis of primary synchronous tumours in 18 % of cases using the presence of adjacent precursor lesions (adenomatous) in both tumoural locations. For all the other cases (82 %) differences in p53 status are helpful for final diagnosis.
Conclusion: Although important for staging and treatment, identifying of synchronous colonic carcinomas, is usually difficult, requiring immunohistochemical criteria.

PS-13-021
The importance of immunohistochemistry in the diagnosis of GISTs
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Objective: A few decades ago, gastrointestinal stromal tumours (GISTs) were diagnosed as tumours of smooth muscle or neural tumours of the gastrointestinal tract, such as leiomyoma, leiomyosarcoma or schwannoma. The aim of this study was to evaluate how the evolution of immunohistochemistry helped us improve our diagnosis of GISTs.
Method: A retrospective study was performed on two different periods of time (both 5 years long): 1996–2000 and 2012–2017, in order to identify patients with GISTs. We analyzed the morphological characteristics and the immunohistochemical profile of these tumours.
Results: In the first group of patients (1996–2000) we have identified 8 potential cases of GISTs diagnosed back then as: schwannomas, leiomyoblastomas, leiomyosarcoma, neurofibroma and ganglioneuroblastoma. On the other hand, in the second group, we have identified 33 patients with GIST. All of them were CD117 positive and 20 of them, CD34 positive.
Conclusion: It is possible that the incidence of GISTs has increased in the past two decades too, but it is clear that immunohistochemistry, in our case the c-kit, is crucial for the precise diagnosis of GISTs.

PS-13-022
Pancreatic metastasis from clear cell renal carcinoma: Report of 3 cases
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Objective: Clear cell renal carcinoma (ccRCC) has a high metastatic capacity, with 30 % synchronous and up to 50 % metachronous presentation; pancreatic metastasis are rare (1.6–11 %), usually occurring several years after nephrectomy. Diagnosis may not be straightforward, especially in the absence of clinical background.
Method: Three male patients, between 57 and 70-years-old, presented with pancreatic nodules, two in the head and one in the tail, well-defined and hypervascular. One patient with head lesion had a total of 9 nodules. Two patients had previous nephrectomy 6 years before for ccRCC.
Results: All nodules had solid and alveolar pattern, composed by clear cells with wide cytoplasm, small nuclei and rare mitotic figures, without lymph node metastasis. Immunohistochemistry: positivity for CD10 and vimentin; negativity for synaptophysin and chromogranin A. Investigation discovered that the patient without background had been subjected to nephrectomy 6 years before for ccRCC. The final diagnosis of ccRCC pancreatic metastasis was made. The patient with 9 nodules had brain metastasis 6 months after surgery and was lost to follow-up. Remaining patients are alive without tumour relapse.
Conclusion: Pancreatic metastases are commonly the only location for ccRCC. Pathological differential diagnosis can be extensive, but conjugation of morphology, immunhistochemistry and clinical background provide the answer.

PS-13-023

Solitary polypoid ganglioneuroma associated with tubular adenoma

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Objective: Ganglioneuromas are mesenchymal polyps of gastrointestinal tract that occur rarely. Intestinal ganglioneuromas have been analyzed in 3 groups: solitary polypoid ganglioneuroma, ganglioneuromatosis polyposis, and diffuse ganglioneuromatosis. The solitary polypoid ganglioneuroma is the most common type and realized incidentally on colonoscopy. However, it is indistinguishable from conventional adenomas clinically.
Method: A 65-years-old male patient , had anemia on routine laboratory tests, underwent colonoscopy. Two polyps, that were 0.7 cm and 0.5 cm in diameter were seen in rectum and removed for histopathological assessment.
Results: Microscopic examination of an H&E stained slides the first polyp showed a large number of ganglion cells which had large and oval eosinophilic cytoplasm, eccentrically placed nucleus and prominent nucleolus in submucosa. However, there were many spindle shaped cells among the ganglion cells. Lesion margins were well-defined and the base of the polyp was intact. Synaptophysin expression were noted in ganglion cells Neuron specific enolase (NSE) and S100 protein marked both ganglion and spindled cells. Other polyp was diagnosed as tubular adenoma with high-grade dysplasia.
Conclusion: We present a rare case of a solitary polypoid ganglioneuroma associated with a conventional adenoma located in rectum.

PS-13-024

Histological characterisation of ipilimumab-associated colitis and enterocolitis - a series review

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Objective: To characterize the histological features in patients with ipilimumab-related colitis.
Method: We reviewed consecutive biopsies and one surgical specimen from patients who developed gastrointestinal symptoms after treatment with ipilimumab between October 2014 and August 2016. We evaluated the presence of intraepithelial neutrophilic leucocytes (IENL), crypt distortion, cryptitis, crypt abscesses, apoptosis, ulceration, granulomas and lymphoplasmacytosis.
Results: There were 6 patients (5 men) diagnosed with ipilimumab-induced colitis. The mean age was 70. Two patients were biopsied twice and one of them also had a subsequent colectomy, i.e. with 9 specimens in total for evaluation. All patients had IENL, with exception of one that showed increase in apoptosis as an isolated alteration. The samples showed crypt distortion (6), cryptitis (7), crypt abscesses (5), apoptosis (8) and plasmacytosis (7), granulomas (1). Ulceration was seen only in the colectomy specimen.
Conclusion: Literature on GI histology related to Ipilimumab CTLA-4 inhibitor is scanty. The histological inflammatory pattern of ipilimumab-induced colitis could mimic GVHD, infectious colitis, IBD or autoimmune enteropathy. Pathologists should consider the diagnosis in new onset diarrhoea occurring in patients with a prior history of melanoma or autoimmune disease and be aware of the spectrum of histological features. Good clinicopathological correlation is important in establishing this diagnosis.

PS-13-025

Human Helicobacter heilmannii-like organisms infection

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Objective: Helicobacter Heilmannii (HHLO) is a bacterial agent with a rare occurence in humans (0.1–2 %) and colonizes especially the antrum.
Method: We present a retrospective analysis of a series of 62 cases with HHLO gastric infection, registered at Fundeni Clinical Institute and at Brescia Civil Hospital, compared with 62 Helicobacter Pylori gastritis cases (HP).
Results: HHLO was found more frequently in young patients (less than 50 years of age), with a slight predominance in males (70.97 % HHLO, compared to 59.68 % HP). All patients presented chronic active gastritis. HHLO seemed to determine less intensity of chronic inflammation (80.65 % moderate and 19.35 % mild HHLO, respectively 88.71 % moderate and 11.29 mild HP). Severe activity was found in 3 of the 62 HHLO cases, compared with 17 HP cases. Mild activity was observed in 26 HHLO and in only 13 HP cases. 4 of the HHLO cases had glandular atrophy, while 6 of the HP ones had. Intestinal metaplasia was observed in 3 HHLO and in 17 HP cases. Only 3 HHLO cases had follicular gastritis compared with 15 HP cases. There was one case with associated HHLO and HP infection.
Conclusion: This is a large series of HHLO infection in humans. It predominates in males and younger patients, and determines a less severe inflamamation than HP. Atrophy is similarly diagnosed, but intestinal metaplasia is rarely observed in HHLO infection. Follicular gastritis is more frequently associated with HP infection.

PS-13-026

Incidence of histopathological lesions of gastric mucosa in obese patients submitted to laparoscopic sleeve gastrectomy

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Objective: To evaluate the incidence of histopathological lesions in surgical specimens obtained through laparoscopic sleeve gastrectomies (LSG) from patients with Body Mass Index (BMI) ≥ 35 and to analyze their association with clinical data
Method: 103 of LSG (27 males, 76 females; mean age: 42,02; mean BMI 43,80) were retrieved from our archive. Haematoxylin and eosin and Giemsa stained slides were reviewed for all cases. Clinical data were obtained through revision of clinical records
Results: 58 (56,3 %) cases had histopathological lesions: gastritis (55 cases; inactive in 31, mild active in 3 and moderately/severely active in 21), hyperplastic polyp (1 case), foveolar hyperplasia (1 case), microcystic dilatation of oxyntic glands (1 case). Helicobacter pylori (HP) was evidenced in 35 (63,6 %) cases and intestinal metaplasia in 2 (3,6 %). The presence of gastric lesions significantly correlated with higher age of the patients (P = 0,034)
Conclusion: The presence of gastric histolopathological lesions, their type and severity is not correlated with sex, BMI and hypercholesterolemia in obese patients submitted to LSG. The age of the patients is the only clinical parameter associated with gastric injury. This suggests that other factors should be investigated to explain the higher incidence of gastric cancer and pre-neoplastic lesions observed in obese patients.

PS-13-028

Ulcerative colitis: Arguments in favour of a composite, histologic, endoscopical and clinical, score for dynamic evaluation of patients

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Objective: Since ulcerative colitis (UC) is a longstanding disease with variable and unforeseeable evolution, there is more and more important the need for a reliable score for dynamic evaluation of patients. Clinical and endoscopical scores fail to evaluate histologic remission, frequently minimizing the risks for relapse and unfavorable evolution, while histologic scores are not well correlated with clinical evolution and with life quality reported by patients.
Method: We prospectively evaluated 45 patients with UC that underwent yearly complete clinical, endoscopical and histologic evaluation. Various histologic and immunohistochemical features were correlated with patients outcome in order to identify the most significant candidates for a composite score.
Results: Geboes histologic score correlated well with Mayo clinical and endoscopical score endoscopic (t test two-tailed 0.0006), but failed to correlate with patients evolution. Persistence of eosinophils and basal plasmacytosis, in inactive lesions, is significantly correlated with relapse risk. Architectural distortion is correlated with p53 and p21 overexpression and with risk of dysplasia.
Conclusion: Some histologic and immunohistochemical parameters, easy to evaluate, can be included in UC scores in order to improve their prognosis value.

PS-13-029

SPEM in gastrectomy specimens of patients with gastric adenocarcinoma: Correlation with clinicopathologic variables

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Objective: SPEM (spasmolytic polypeptide-expressing metaplasia) is a metaplastic mucous cell lineage with phenotypic characteristics of antral gland cells within oxyntic mucosa. SPEM has been found to be retalted with gastric adenocarcinoma (GCa) as strongly as intestinal metaplasia (IM). Also, in some mouse models of GCa, SPEM increased the risk of GCa, dramatically.
Method: Partial/total gastrectomy specimens of patients with GCa between 2015 and 2016, in Marmara University Department of Pathology, were included in the study. Characteristics of patients, tumour and non-neoplastic gastric mucosa were noted from pathology reports.
Results: Our study included 189 patients with a mean age of 63.8. Frequencies of SPEM, IM, Paneth metaplasia(PCM), and H. Pylori(HP) were 14 , 50 , 52 , and 39 %, respectively. Mean age was higher in SPEM(+) cases (67.4) than SPEM (-) ones (63.2) ($p > 0.05$). SPEM was more frequent in HP(+) ($p < 0.05$), multifocal atrophy ($p < 0.05$), İM ($p < 0.05$), PCM ($p < 0.1$). All SPEM(+) cases had IM, except one. localisation of the tumour had no effect on the presence of SPEM. Results of the logit model showed a statistically significant relationship between PCM, HP and SPEM (both $p < 0.1$). Controlling for all other factors, probability of observing SPEM increased from 11 to 21 % in HP (+) cases, as compared to HP(-) ones.
Conclusion: Our study indicated that SPEM may represent a precursor for development of intestinal metaplasia, and it is closely associated with HP. But our data is limited to support SPEM, as the precursor lesion for GCa.

PS-13-030

Statistical analysis of small bowel lesions presenting as tumours

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Objective: Although the small bowel represents 75 % of the length and 90 % of the surface area of the gastrointestinal tract, small intestine neoplasms are 40–60 times less common than colonic ones.
Method: We made a retrospective analysis of small bowel tumours registered at Victor Babes National Institute of Pathology between 2007 and 2017 and at Fundeni Clinical Institute between 2011 and 2016.
Results: We identified 63 cases that matched the criteria, out of which 27 (42.86 %) were female patients and 36 (57.14 %) were male patients. The ages ranged between 1 and 80 years old, with an average age of 51 years-old. The most frequent lesion was gastric heterotopia (fundic glands), found at 31 % (20/63) of the patients. Gastrointestinal stromal tumours were the second most frequent lesions, representing 22 % (14/63) of cases, while adenocarcinomas represented 9.5 % (6/63) cases, like lymphoid nodular hyperplasia. The 5th most frequent finding was Brunner gland hyperplasia, found in 8 % (5/63) of cases, out of which 3 were associated with gastric heterotopia. 3 cases of non-Hodgkin malignant lymphoma and 3 of adenomatous polyps were identified. There were 2 cases with NETG1, 1 lymphatic ectasia, 1 leiomysarcoma, 1 hyperplastic polyp and only 1 case of undifferentiated malignant tumour.
Conclusion: Small intestine growths may be neoplastic or non-neoplastic lesions and may be equally discovered in small intestine biopsies or excision specimens.

PS-13-031

Short-term histopathological response to anti-tumour necrosis factor alpha therapy in patients with ulcerative colitis

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Objective: Predicting short-term efficacy of anti-tumour necrosis factor alpha (anti-TNFα) treatment by analysing the histopathological aspects of colon biopsy in patients with chronic active ulcerative colitis (UC).
Method: Colonoscopy was performed on patients with active UC diagnosed in Colentina University Clinical Hospital between 2012 and 2014 and biopsies were obtained from the most affected area of the colon or rectum, for histological evaluation, according to the method described by Geboes, before beginning the anti-TNFα treatment and after 6 to 12 months of therapy.
Results: The study included 13 patients, 9 males with ages between 31 and 63 and 4 females with ages between 19 and 42 years old. A clear improvement in the histological score was observed after the treatment. The average Geboes score had a significant decrease ($p = 0.03$) from 5 at baseline, to 4 at the final of the study. The grade of crypt destruction decreased form an average of 1.46 to 0.84 ($p = 0.04$). The grade of erosion/ulceration was reduced after therapy ($p = 0.01$) and the number of epithelial apoptotic bodies diminished ($p = 0.05$).
Conclusion: The results provide evidence that the administration of anti-TNFα therapy rapidly reduces epithelial lesions and remodelling, response that is more significant on short-term than dissolution of inflammation.

PS-13-032

Rare osseous metaplasia in left colonic adenocarcinoma: Case report

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Objective: Osseous metaplasia is a rare entity in gastrointestinal tract malignancies. Moreover, ossification is extremely rare in colorectal carcinoma and the responsible mechanisms are not completely understood. Here, we report the case of a 70 year old woman with osseous metaplasia in colonic adenocarcinoma.
Method: A 70 year old woman presented to our hospital with a 2 month history of weight loss and abdominal pain in left iliac fossa. Colonoscopy revealed a circumferential, exofitic and infiltrative tumour 25 cm from the anus. A tumour biopsy indicated a moderately differentiated invasive adenocarcinoma. Laboratory data (carcinoembryonic antigen – 2,78 ng/mL and carbohydrate antigen 19−9–4,1 u/mL) were within normal range. Abdominal computed tomography showed a left colonic tumour with calcified deposits. Therefore, Reybard sigmoidectomy was performed under general anesthesia.
Results: The resected specimen showed a circumferential, polypoid and infiltrative tumour (2,5/2,3/1,5 cm) with superficial ulceration, situated 2 cm from the distal margin. Histologically, the tumour was moderately differentiated adenocarcinoma extending through the muscularis propria into the subserosal tissue. The tumour contained numerous foci of well-formed bony trabeculae within the stroma composed of osteoid and ossification with osteoblastic rimming. One of 14 dissected lymph nodes had metastatic adenocarcinoma without metaplastic ossification. The patient's postoperative clinical course was uneventful and 3 months after surgery she showed no signs of recurrence.
Conclusion: Colon cancer is a common disease, but coincidental osseous metaplasia is a very rare entity. The most plausible explanation - a metaplastic process of stromal mesenchymal cells into osteoblasts—is yet to be demonstrated. Further studies are necessary to determine the factors that play a key role in this mechanism.

PS-13-033
Helicobacter pylori - not a lonely player in gastric carcinogenesis
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Objective: Helicobacter pylori(HP) is considered the most important factor that triggers and maintains the evolution towards gastric adenocarcinoma in patients with chronic gastritis. This study evaluates correlations between Helicobacter pylori (HP) infection and pre-malignant changes of gastric epithelium.
Method: We present a retrospective study including 153 cases of chronic gastritis with associated dysplasia, 62 males and 91 females, aged 25 to 92, with no previous anti-HP treatment. In 85 cases (55.56 %), patients presented HP infection with different density levels (62.74 % - low, 24.18 % - medium, 13.08 % - high).
Results: Only 16.34 % of the non-infected patients presented both atrophy and metaplasia, while 24.18 % of the infected ones had those histopathologic changes.Most cases without HP had inactive gastritis, while 69.93 % of the infected had highly active gastritis.Only 10 patients with intestinal type gastric adenocarcinoma, all infected.High-grade dysplasia (including globoid type) was less associated with atrophy and metaplasia, but more with their absence in gastritis with HP.
Conclusion: HP is not the only factor involved in the development of intestinal type gastric adenocarcinoma. Other factors are inducing similar pre-malignant changes and only HP-eradication is not sufficient to cease carcinogenesis cascade.

PS-13-034
A 14-year-old child with alopecia areata presenting inflammatory bowel disease (Crohn's disease)
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Objective: Alopecia Areata (AA) is a non-scarring hair loss, in which the characteristic initial lesion is a well-circumscribed bald patch. There are rare cases associating AA with Crohn's disease, especially in young patients.
Method: We report the case of a 14-year-old boy presenting with abdominal pain, chronic diarrhea, weight loss (17 kg in 3 months) and AA. The symptoms appeared 3 months prior to the presentation. He previously had another episode of AA, treated topically, with favorable evolution.
Results: Biochemical investigations revealed an important inflammatory syndrome, which persisted during and after antibiotic treatment. Because of abdominal symptoms, a total colonoscopy was performed, revealing hyperemia, edema and aphthoid lesions. Microscopically, the biopsies taken displayed chronic active colitis, transmucosal, aphthoid erosions above lymphoid nodules, pericriptic epithelioid granulomas with multinucleated giant cells and lymphonodular hyperplasia. After excluding a specific infection, as well as other diseases, the diagnosis of Crohn's disease was established. Specific treatment was initiated, with a good clinical response and remission of alopecia after 4 months of treatment. After 16 months, other colonic biopsies were taken, revealing focal active colitis and small epithelioid granulomas.
Conclusion: It is unknown if AA was an early extraintestinal manifestation of a silent Crohn's disease, if it was the other way around, or if their development was independent from one another.

PS-13-035
High expression of Aldolase B confers a poor prognosis for rectal cancer patients receiving neoadjuvant chemoradiotherapy
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Objective: Colorectal cancer is the fourth most common cause of cancer mortality. For rectal cancer, neoadjuvant concurrent chemoradiotherapy (CCRT) followed by radical proctectomy is gold standard treatment for patients with stage II/III rectal cancer. By data mining a documented database of rectal cancer transcriptome (GSE35452) from Gene Expression Omnibus, National Center of Biotechnology Information, we recognized that ALDOB was the most significantly up-regulated transcript among those related to glycolysis (GO: 0006096). Hence, we analyzed the clinicopathological correlation and prognostic effect of ALDOB protein (Aldolase B), which encoded by ALDOB gene.
Method: ALDOB immunostain was performed in 172 rectal adenocarcinomas treated with preoperative chemoradiotherapy followed by radical surgery, which were divided into high- and low-expression groups. Furthermore, statistical analyses were examined to correlate the relationship between ALDOB immunoreactivity and important clinicopathological characteristics, as well as three survival indices: disease-specific survival (DSS), local recurrence-free survival (LRFS) and metastasis-free survival (MeFS).
Results: ALDOB (Aldolase B) over-expression was significantly associated with pre-CCRT and post-CCRT tumour advancement, lymphovascular invasion, perineural invasion and poor response to CCRT (all $P \leq .023$). In addition, ALDOB high expression was linked to adverse DSS, LRFS and MeFS in univariate analysis (all $P \leq .0075$) and also served as an independent prognosticator indicating dismal DSS and MeFS in multivariate analysis (all $P \leq .019$).

Conclusion: Aldolase B may play an imperative role in rectal cancer progression and responsiveness to neoadjuvant CCRT, and serve as a novel prognostic biomarker. Additional researches to clarify the molecular and biochemical pathways are essential for developing promising ALDOB-targeted therapies for patients with rectal cancers.

PS-13-036

High immunoreactivity of DUOX2 is associated with poor response to preoperative chemoradiation therapy and worse prognosis in rectal cancers

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Objective: Colorectal cancer ranks as the fourth most common cause of cancer mortality worldwide. For rectal cancer, neoadjuvant concurrent chemoradiotherapy (CCRT) followed by radical proctectomy is common. By data mining a documented database of rectal cancer transcriptome (GSE35452) from GEO, NCBI, we recognized that DUOX2 was the most significantly up-regulated transcript among those related to cytokine and chemokine mediated signaling pathway (GO:0019221). Hence, the aim of this study was to assess the DUOX2 expression level and its clinicopathological correlation and prognostic significance in patients of rectal cancer.
Method: DUOX2 immunostain was performed in 172 rectal adenocarcinomas treated with preoperative CCRT followed by radical proctectomy, which were divided into high- and low-expression subgroups. Furthermore, statistical analyses were examined to correlate the relationship between DUOX2 immunoreactivity and important clinicopathological features, as well as three survival indices: disease-specific survival (DSS), local recurrence-free survival (LRFS) and metastasis-free survival (MeFS).
Results: DUOX2 overexpression was linked to post-CCRT tumour advancement, pre- and post-CCRT nodal metastasis and poor response to CCRT (all $P \leq 0.021$). Furthermore, DUOX2 high expression was significantly associated with inferior DSS, LRFS and MeFS in univariate analysis ($P \leq 0.0097$) and also served as an independent prognosticator indicating shorter DSS and LRFS interval in multivariate analysis ($P \leq 0.01$).
Conclusion: DUOX2 may play a pivotal role in carcinogenesis, tumour progression and response to neoadjuvant CCRT in rectal cancers, and serve as a novel prognostic biomarker. Additional researches to clarify the molecular and biochemical pathways are essential for developing promising DUOX2-targeted therapies for patients with rectal cancers.

PS-13-037

Chemotherapy or not? Practice changing approach for the accurate selection of patients for chemotherapy treatment after colon cancer diagnosis. The Tumour-Stroma-Ratio (TSR) as addition to the TNM classification

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Objective: The tumour-micro-environment is an important determinant of tumour behaviour. We developed a new, easy to apply, practice changing method to select colon cancer patients for adjuvant therapy: the tumour-stroma ratio (TSR). The current proposal aims to prepare implementation of this method by training international pathologists and prospective validation of the parameter in an international setting.
Method: 1. A reproducibility study on TSR scoring in H&E stained tumour tissues will be conducted among international pathologists. An e-learning module will be developed with a quality assessment program in the framework of the European Society of Pathology EQA program. 2. Automation of the TSR using whole slide imaging and state-of-the-art pattern recognition techniques. 3. A prospective clinical trial will be performed that evaluates the introduction of the TSR in clinical practice.
Results: The TSR parameter is based on the amount of stroma within the primary tumour resulting in worse patient outcome. The TSR parameter can be determined at routine pathology diagnostics and has an excellent inter-observer agreement with $K > 0.80$. Several cohort studies resulted in significant differences in survival time between stroma-high and stroma-low patients ($p < 0.0001$, HZ 2.5). These results were validated in the VICTOR trial (stage II, III: OS $p < 0.0001$, HR = 1.96; DFS $p < 0.0001$, HR = 2.15) and the Quasar II study (stage II,III: OS $p = 0.003$, HR = 1.53; DFS $p = 0.001$, HR = 1.53).
Conclusion: Standardization and prospective validation of TSR will result in inclusion of the parameter in the TNM classification leading to more accurate decision making for adjuvant chemotherapy.

PS-13-038

Prognostic value of N1c after neoadjuvant radiochemotherapy in rectal cancer

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Objective: The indication of adjuvant chemotherapy for pN1c patients in rectal cancer after neoadjuvant radiochemotherapy is still debated although the prognostic value of tumour deposit (TD) has been clearly demonstrated . This study aimed to determine the prognosis of ypN1c patients compared to ypN0 and ypN+ patients without TD.
Method: We examined clinicopathological features of rectal cancer among 265 consecutive patients from 2005 to 2013. We calculated 3 years overall survival (OS), disease free survival (DFS), local and distant DFS of ypN1c ($n = 19$, 7 %), ypN0 ($n = 161$; 61 %) and ypN+ ($n = 40$; 15 %) without TD, patients.
Results: After a median follow up of 40 months, 3 years OS was significantly lower in ypN1c compared to ypN0 ($p = 0.03$) and ypN+ ($p = 0.038$) patients. There were no significant differences in term of DFS, local and distant DFS between groups. However, the rate of synchronous distant metastasis was higher in ypN1c than in ypN0 groups (27 % vs 2 %, $p = 0.0001$) and was not different compared to ypN+ group (27%vs 11 %, $p = 0.25$).
Conclusion: ypN1c patients appear to have a more aggressive profile than ypN0 patients and could justify the implementation of adjuvant chemotherapy as ypN+ patients.

PS-13-039

Tumour-Stroma-Ratio (TSR) holds important information when stratifying stage II colon cancer patients into high and low risk groups, a population based study

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Objective: Despite the well-known uncertainty on efficiency, adjuvant chemotherapy is today offered to a subgroup of stage II colon cancer patients. Recent research focusing on the stroma in epithelial tumours has shown that patients with a high percentage of stroma within the tumour, determined by the Tumour-Stroma-Ratio (TSR), harbour a poor prognosis.
Method: The study included all patients diagnosed with stage II colon cancer in Denmark in 2003. Stroma-high (>50 % stroma) and stroma-low (≤50 % stroma) groups were evaluated regarding Overall Survival (OS) and Recurrence-Free Cancer Specific Survival (RF-CSS).
Results: TSR showed prognostic impact in both univariate (OS: $p = 0.0075$, HR = 1.58 (1.14–2.20), RF-CSS: $p < 10{-}5$, HR = 2.47 (1.53–3.98)) and

multiple COX analyses (OS: $p = 0.0007$, HR = 1.66 (1.24–2.22), RF-CSS: $p = 0.0001$, HR = 2.22 (1.58–3.27)). When stratifying according to TSR, stroma high patients (107 (18.4 %)) showed significantly poorer 5 years RF-CSS in both low (stroma high: 76 %, stroma low; 89 %; $p < 10{-}5$) and high (stroma high: 49 %, stroma low: 71 %; $p = 0.01$) risk groups.
Conclusion: This population based study confirms the prognostic importance of TSR, and calls for including TSR in the current risk assessment of patients with stage II colon cancer, in order to a more appropriate definition of high and low risk groups than todays practice.

PS-13-040
Expression of epiregulin and amphiregulin in colorectal cancer cells and their microenvironment
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Objective: To evaluate mRNA and protein expression of amphiregulin (AREG) and epiregulin (EREG) in colorectal cancer cells and surrounding stromal cells.
Method: AREG and EREG mRNAs and proteins were examined by real-time PCR and immunohistochemistry respectively, in cancer cells and stromal cells obtained with laser microdissection from 23 colorectal cancers.
Results: AREG and EREG expression in cancer cells and stromal cells was detected in all cases, and mRNA in almost all cases. In all cases the expression of AREG and EREG protein was higher in tumour cells than in the stromal cells. A strong correlation was found between protein and mRNA expression of the ligands in the cancer and stromal cells and between the expression of AREG and EREG proteins and mRNAs in cancer cells. Significant correlation was found between the expression of the AREG and EREG protein and the location of tumours.
Conclusion: 1. The cancer cells are the primary source of AREG and EREG in tumour microenvironment. 2. The mutual regulation of the expression of AREG and EREG in the stromal and cancer cells supports the hypothesis of paracrine communication between these cell populations. 3. The correlation between the expression of the AREG and EREG protein and the site of the tumour supports the hypothesis of biological differences between proximal and distal colon cancers.

PS-13-041
Dynamics of genetic aberrations in Crohn's disease associated colorectal carcinogenesis
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Objective: Crohn's disease, a condition of chronic inflammation of the intestine, significantly increases the risk for the development of colorectal cancer (CRC). Sporadic CRCs are characterized by a specific pattern of genomic imbalances and a landscape of acquired gene mutations. In this study we aimed to compare CRCs associated with Crohn's disease with sporadic CRCs.
Method: We analyzed 26 Crohn's disease associated CRCs, four matched dysplastic lesions, six matched inflamed mucosa samples, and two matched lymph node metastases using array comparative genomic hybridization and targeted sequencing (563 cancer related genes). As a control, we used normal intestinal mucosa from the resection margin of these CRCs and 24 sporadic CRCs.
Results: In general, CRCs that developed in patients with Crohn's disease mainly showed chromosomal aberrations expected in CRC. However, we identified the following distinct mutation signature compared to sporadic CRC: TP53 (65 % in Crohn's disease associated CRC versus 33 % in sporadic CRC), KRAS (27 % versus 54 %), APC (23 % versus 75 %), PIK3CA (19 % versus 8 %), SMAD4 (12 % versus 13 %) and SMAD3 (4 % versus 29 %). The genetic analyses of multiple lesions from individual patients revealed a high degree of intertumoural heterogeneity with diverse patterns of gene mutations and allowed reconstruction of the sequence of genetic events during Crohn's disease associated tumourigenesis.
Conclusion: Our comprehensive molecular profiling of Crohn's disease associated CRCs suggests that the genetic landscape of CRC is influenced by the activation of inflammation related pathways. Furthermore, our findings offer potential for establishing an early detection marker for dysplasia in patients with Crohn's disease.

PS-13-042
Colorectal carcinoma (CRC) stage II: Evaluation of CDX2 expression and microsatellite instability (MSI) as potential biomarkers
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Objective: CDX2 expression and MSI have been proposed as prognostic biomarkers in CRC. We investigated 173 cases CCR stage II in order to clarify their potential role for selecting high risk subgroup.
Method: Surgical tumour samples of 173 patients, retrospectively collected, were immunostained for CDX2 and DNA extraction was carried out for MSI analysis. In MSI+ samples mismatch repair proteins (MMR) expression and BRAF exon15 sequencing were performed. CDX2 staining was scored as weak-moderate or intense according to intensity of staining and percentage of positive cells.
Results: 33/169 (19 %) showed MSI (mean age 66y). In 12/173 (7 %) samples complete loss of CDX2 expression was observed; 40 (23 %) and 121 (70 %) samples showed weak or strong CDX2 expression respectively. CDX2 loss was associated with MSI (90 %), proximal location (90 %), BRAF V600E mutation (60 %), old age (mean age 72y). In 60 % of CDX2+ samples we observed a reduction/absence of CDX2 on tumour budding.
Conclusion: CDX2 expression seems to identify a specific subgroup of CRC in the stage II related to sporadic MSI. The observation of CDX2 reduction on tumour budding suggests a possible role on epithelial mesenchimal transition. Prognostic value of CDX2 loss and its expression in budding is under investigation in our series.

PS-13-043
Ectopic crypts are common in large tubular and tubulovillous adenoma, not specific for traditional serrated adenoma
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Objective: Traditional serrated adenoma (TSA) refers to a subtype of serrated polyps with exophytic configuration, villous growth pattern, and eosinophilic cytoplasm. Formation of ectopic crypts due to loss of crypt anchoring to the muscularis mucosae is considered a specific feature for TSA. Our study challenged this concept and showed presence of ectopic crypts in a significant proportion of tubular/tubulovillous adenomas.
Method: Total 316 tubular, tubulovillous and villous adenomas were studied. Adenomas were grouped according to polyp size: < 0.5 cm; 0.5 to 1 cm; 1 to 2 cm and > 2 cm. Ectopic crypt was defined as abnormal crypt with loss of orientation and no abutting of crypt base to muscularis mucosae. A chi-squared test was used for statistical analysis.
Results: Ectopic crypts were identified in 27.5 % colonic tubular/tubulovillous adenomas. The presence of ectopic crypts is correlated with larger size and villous architecture of adenomas (8.9 % in <0.5 cm group; 14.8 % in 0.5–1 cm group; 84.6 % in 1–2 cm group; 100 % in >2 cm group; $P < 0.001$). There is no significant difference between polyp location and ectopic crypt expression.

Conclusion: Our study indicates that ectopic crypt formation is common in colonic tubular/tubulovillous adenomas, especially adenomas with larger size and villous architecture. Ectopic crypt is not specific for TSA.

PS-13-044

Inter-observer agreement of the Paris classification in pT1b esophageal adenocarcinoma

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Objective: To evaluate the inter-observer agreement (IOA) of the Paris classification (sm1 ≤ 500 μm and sm2/3 > 500 μm) for the assessment of submucosal (pT1b) tumour invasion.
Method: All patients with pT1b esophageal adenocarcinoma (EAC) treated by either endoscopic resection (ER) or primary surgery between 1989 and 2014, were identified from a tertiary referral center. H&E slides and additional desmin and pankeratin (D&P) double stained slides were independently reviewed by three expert GI-pathologists, blinded for the original diagnosis and clinical outcome. The deepest level of invasion was recorded in μm by each pathologist. The IOA was determined using the intraclass correlation coefficient (ICC) for continuous variables and Fleiss' kappa (κ) for categorical variables.
Results: In total, 78 patients were included, 34 treated by ER and 44 by primary surgery. When determining the depth of submucosal invasion in μm, the IOA was good (ICC = 0.64, 95 % CI 0.52–0.74) in H&E-slides, and good (ICC = 0.76, 95 % CI 0.63–0.86) in D&P-slides. When slides were assessed according to the Paris classification, the IOA was good (κ = 0.63, 95 % CI 0.50–0.76).
Conclusion: There is good agreement between expert GI-pathologists in determining the exact depth of sm invasion in pT1b EAC, which is essential for the treatment strategy and prognosis after a complete ER of a lesion.

PS-13-045

Regulation of CDX2 in colorectal cancer via methylation and histone deacetylation?

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Objective: In stage II and III colorectal cancer (CRC) CDX2 is a diagnostic, prognostic and potentially predictive biomarker. Aberrant expression of the CDX2 gene, detected in approximately 20 % of CRCs, is associated with tumourigenesis. The aim of the study was to restore CDX2 by targeting epigenetic modifications.
Method: Two CDX2-negative CRC cell lines, Colo-205 and SW-620 were treated with increasing concentrations of DNA methyltransferase inhibitor (DNMTi), Decitabine alone and combined with the Histone deacetylase inhibitor (HDACi) Trichostatin A (TSA), as well as HDAC4 inhibitor LMK-235 and HDAC1 and HDAC2 inhibitor Romidepsin. CDX2 restoration was assessed by western blot, qPCR and immunohistochemistry (IHC).
Results: After treatment with Decitabine a significant dose-dependent 15-fold increase of CDX2 mRNA and protein were detected. Additionally synergistic effects of Decitabine and TSA treatment were observed with a 150-fold increase of CDX2 mRNA upregulation and protein level. Further evaluations revealed synergistic effects of Decitabine in combination with LMK-235 and Romidepsin showing an up to 35-fold and 30-fold increase of CDX2 mRNA, respectively.
Conclusion: Methylation and histone deacetylation may play a major role in CDX2 regulation. Targeting specific HDAC's or DNMT's involved in the epigenetic regulation of CDX2 could provide an alternative treatment possibility for patients with CRC.

PS-13-046

Systematic prospective screening of eosinophilic oesophagitis in a cohort of 63 adolescents with oesophageal atresia

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Objective: The esophageal atresia (EA) is the most frequent congenital malformation of the oesophagus. Eosinophils infiltration of the esophageal mucosa seems frequently associated with EA, and could be mainly explained by gastroesophageal reflux disease (GERD) or by eosinophilic oesophagitis (EoE). The aim of this study was to investigate the prevalence of EoE among EA adolescents and to describe characteristics of those patients.
Method: Routine upper gastrointestinal endoscopy with esophageal biopsies was performed prospectively in a series of 63 patients for systematic follow-up. EoE was identified in patients with one or more biopsy specimens displaying ≥ 15 intraepithelial eosinophils per one high power field (/HPF) who was treated with Proton pump inhibitors (PPIs) for at least 4 weeks.
Results: Six patients presented 17 to 100 eosinophils/HPF, 3 of them having a proven EoE. All EoE patients had a history of allergy at time of diagnosis.
Conclusion: Three adolescents (4.7 %) of 63 patients with EA had a proven EoE, which higher than expected in the general population (0.89 to 4/10 000). A history of allergy should lead to the suspicion of EoE and to achievement of biopsies.

PS-13-047

Morphological characteristics of a three dimensional in vitro model for individualised colorectal cancer chemotherapy

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Objective: There is an emergent need for valid in vitro models to investigate the effect of individualized chemotherapy regimen for cancer patients. For this purpose, a functional in vitro 3D model based on the patient's own cancer tissue (i.e. a tumouroid) has successfully been established by 2cureX. This study investigated the 3D model for its morphological characteristics and demonstrated an innovative 3D reconstruction technique.
Method: Tumouroids were cultured and grown in hydrogel matrix for 15 days prior to fixation and embedding. Sections were PAS stained and stained immunohistochemically for Ki67, active caspase 3 and CK20. Furthermore, 3D figures of tumouroids were reconstructed by aligning the virtual slides in ImageJ software.
Results: The tumouroids increased their size more than 10-fold when cultured for 15 days resulting in tumouroids exceeding 500 μm in diameter. CK20 and PAS stain confirmed the epithelial and glandular nature of the tumouroids, and Ki67 and active caspase 3 stains demonstrated that the tumouroids were made from proliferating cells with minimal apoptosis. The 3D reconstruction demonstrated a non-symmetric anatomy.
Conclusion: Tumouroids based on the patient's own cancer cells appear to be good candidates for chemosensitivity assays in relation to personalized anti-cancer treatment.

PS-13-049

Topography immunohistochemical markers in pancreatic ductal adenocarcinoma: Application of CDX2, CK7,CK19, CK20, MUC1, CEAm and CA19.9

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Objective: Pancreatic cancer is one of the most aggressive and chemoresistant tumour. Identification topography of diagnostic antibody is important for diagnosis of this disease.
Method: We investigated the expression patterns of MUC1, CDX2, CEAm, CK7, CK19, CK20, and CA19.9 in 288 cases of pancreatic ductal carcinoma using TMA technology. TMA spots were taken from different part of resection specimen: central and periphery part of the tumour and metastasis, if was presented.
Results: The expression of CA19.9 and CK7 was similar in all parts of tumour. The positive expression rate was high and comparative for CK 7, MUC 1, CK 19. and CA19.9 (over 80 %). Expression of CEAm was less then 70 % in central part and in only 37,5 % in metastasis. Lowest levels of expression CDX2 and CK20 allow us include this markers in to differential panel.
Conclusion: According to our data following markers can prove pancreatic ductal carcinoma: MUC1, CK19 and CK7 as a strong and CA19.1 and CEAm was weaker markers and it is necessary to include in panel CDX2 and CK20 with negative expression pattern.

PS-13-051

Comparison of the efficiency of transgelin, smodthelin, smooth muscle myosin and CD31 antibodies for the assessment of vascular tumour invasion and free tumour deposits in gastric, pancreatic and colorectal adenocarcinomas

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Objective: This study aimed to compare CD31, smoothelin, smooth muscle myosin (SMM) and transgelin for their efficiency in detecting venous invasion and the nature of free tumour deposits in gastric, pancreatic and colorectal adenocarcinomas.
Method: Eleven Whipple, 5 gastrectomy, 3 colectomy and 1 low anterior resection specimens were reviewed and examined which revealed 254 probable foci. Foci were reviewed and divided into 3 types: Type A, the "orphan artery" pattern; Type F, free tumour deposits in the peri-organal adipose and connective tissue without an unaccompanied artery; and, Type X, a focus which could be detected only with the immunohistochemical procedures mentioned.
Results: No foci were positive by smoothelin and CD31. Transgelin was more sensitive than SMM in all foci types gathered, and A type and F type foci ($p < 0{,}001$, $p = 0$, 001 and $p = 0$, 10, respectively). In free tumour deposits (type F), 35,7 % were negative by all four stains and 64,2 % were positive by SMM and transgelin. We could not make the distinction between metastatic lymph node and venous invasion in positive foci.
Conclusion: We conclude that H&E stain is inadequate and smooth muscle markers like transgelin and/or SMM are more efficient in revealing a venous invasion and probably lymph node / large extramural invasion.

PS-13-052

Association of PDL-1, CDX2 and CD8 expressions with microsatellite instability in colorectal carcinoma cases

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Objective: Programmed cell death 1 (PD-1) and its ligand (PD-L1) regulate tumour immune response. Immun checkpoint blokers offers a promising new therapeutic strategy. In colorectal carcinoma (CRC) the response to PD-1/PD-L1 inhibition is correlated with microsatellite instability. There is limited data about the clinicopathologic profile, prognostic characteristics of CRC and PD-L1 expression
Method: In this study, 108 primary CRC cases were analysed histologically and immunohistochemically for PD-L1, intestinal differentiation marker CDX2, CD8 and molecular Microsatellite instability (MSI) testing,
Results: MSİ-high was detected 26,8 % of all cases. Right colon was observed in 68,9 % of MSI-H cases, although neither of them was located in rectum. Overall PD-L1 expression was 28,5 % of the cases. While PD-L1 was expressed in 11,4 % of MSS cases, it was 47 % in MSİ group ($p < 0.05$). PD-L1 expression was associated with increased number of CD8 positive tumour infiltrating lymphocytes and loss or weak expression of CDX2.
Conclusion: MSI-H CRC cases can have benefit for anti-PD-1/PD-L1 therapy. Also, our findings suggest that CDX2 and PD-L1 expression status could be used as potential prognostic and predictive biomarkers for CRCs

PS-13-053

Clinicopathological aspects and particularities of epithelial-mesenchymal transition in colorectal versus gastric adenocarcinomas

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Objective: To identify the histological and immunohistochemical (IHC) particularities of colorectal (CRC) versus gastric adenocarcinomas (GC).
Method: We have examined 71 consecutive cases of CRC and 160 GCs using the IHC markers E-cadherin, N-cadherin and β-catenin. All of the cases were classified in low- versus high-grade budding tumours.
Results: The budding grade in the invasion front was higher in the GCs than CRCs ($p = 0.003$). In the tumour core, the percentage of E-cadherin positivity was similar in both groups (62.5 % for CRC and 58.33 % for GC); membrane positivity for β-catenin was also similar ($p = 0.66$). In the invasion front, totally loss of E-cadherin was more frequent in the GC buds (54.03 % versus 21.82 %) and β-catenin membrane-to-nuclear translocation was more frequent in CRC than GC buds ($p < 0.0001$). N-cadherin positivity was more frequently seen in the GC than CRC cells ($p = 0.001$) without differences between tumour core and invasion front.
Conclusion: In GC cells, the EMT is indicated by N-cadherin positivity and totally loss of E-cadherin and does not depend on the dyscohesivity grade. In CRC, this process is rather induced by focally loss of E-cadherin and β-catenin translocation and should be quantified in the invasion front.

PS-13-055

Heterotopic pancreas of the gastrointestinal tract and associated precursor and cancerous lesions: Systematic pathological studies of 165 cases

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Objective: The aim is to identify possible progression from precursor lesions to adenocarcinomas in heterotopic pancreas (HP).
Method: We investigated clinicopathological features among 165 resected HPs [gastric (57 cases,35 %), duodenal (56,34 %), omental (30,18 %), and jejunal (22,13 %)].
Results: Symptomatic HPs [79/135 gastrointestinal tract (GIT) wall HPs, 59 %] were larger ($P = 0.05$), more common in younger patients and in a gastric location (both $P < 0.001$), and more frequently associated with lymphoid cuffs ($P = 0.03$) than incidentally found HPs. Gastric/jejunal

HPs were more frequently symptomatic ($P < 0.001$), deeply located ($P = 0.03$), and associated with lymphoid cuffs ($P = 0.008$) and pancreatic-intraepithelial neoplasia/intraductal-papillary-mucinous neoplasms (PanIN/IPMN;$P = 0.001$) than duodenal HPs. HP was frequently associated with acinar-ductal metaplasias (117/135 GIT wall HPs,87 %) and PanINs/IPMNs (68/135,50 %); those with PanINs/IPMNs were larger ($P < 0.001$), more frequently located in stomach ($P = 0.001$), had deeper wall involvement ($P = 0.03$), and more often showed infiltrative growth ($P < 0.001$) and lymphoid cuffs ($P = 0.02$). Four HPs containing PanINs abutted adenocarcinomas, all expressing wild-type KRAS and intact SMAD4/DPC4 expression.
Conclusion: HPs containing PanINs/IPMNs (usually low grade) are larger and more common in stomach and show deeper location, infiltrative growth, and lymphoid cuffs. Adenocarcinomas are rarely observed adjacent to HPs with PanINs/IPMNs. KRAS mutational and SMAD4/DPC4 immunohistochemical studies can discriminate between adenocarcinoma derived from HP and concurrent adenocarcinoma with HP.

PS-13-056
Increased intratumoural infiltrating lymphocytes and CD9a expression in gastric carcinoma
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Objective: The aim of our study was to evaluate the prognostic significance of intratumoural lymphocytes and exosomal marker CD9a as well as clinicopathological characteristics in patients with gastric cancer (GC).
Method: Altogether, 300 patients undergoing GC surgery at Riga East University Hospital in 2012–2014 were retrospectively enrolled in the study. The control group consisted from 20 upper endoscopy biopsy cases. The tissue samples were stained by hematoxylin-eosin and immunohistochemically.
Results: Obtained results showed that the expression of CD9a was increased in GC both intestinal and diffuse type compared to control group (respectively, 1.7 ± 1.28 vs. 0.4 ± 0.5, score, $p < 0.01$ and 2.2 ± 1.08 vs. 0.4 ± 0.5, score, $p < 0.001$). The CD9a expression appeared mostly as a vesicular like staining in the cytoplasm. Furthermore, the increased numbers of infiltrating peritumoural lymphocytes in patients with intestinal type compared to diffuse type of GC was observed. The positive correlation between CD9a expression and disease stage was observed ($p < 0.0001$). In addition, the positive correlation between the degree of differentiation and infiltrating peritumoural lymphocytes was revealed (Rho = +0.72; $p < 0.001$).
Conclusion: To conclude, our data showed increased expression of CD9a in GC, which correlated with disease stage. Furthermore, intratumoural lymphocytes are associated with GC clinicopathological characteristics.

PS-13-057
Acute appendicitis and neurogen appendix: Relevance of morphological features and of WT1 expression
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Objective: The objective of this study was to study neurogen appendix (NAP) cases for relationships between appendicitis features (acute, chronic inflammation, peritonitis) and baseline and immunohistochemical characteristics. NAP is known to interfere with appendix motility and fecal stagnation.
Method: 36 NAP (confirmed by S100 immunohistochemical positivity) were studied for clinico-morphological features as well as for WT1 and Bcl2 immunohistochemistry. The Kendall correlation test was used for the statistical analysis. Logistic regression models were constructed for predicting acute inflammation and presence of peritonitis.
Results: Acute appendicitis (75 % NAP) correlated to age as well as to the presence of inflammatory vascular hiatus, to the lack of submucosal involvement and to the presence of WT1 expression in NAP (Kendall $p < 0.01$/tau = 0.384, $p = 0.02$/tau = 0.272 $p < 0.01$/tau = −0.321 and, $p = 0.04$/tau = 0.240). WT1 and Bcl2 expression in NAP were correlated (Kendall $p < 0.01$/tau = 0.394). Peritonitis (63 % NAP) correlated also to lack of Bcl2 expression in NAP (Kendall $p = 0.03$/tau = −0.265). NAP without submucosal involvement predicted peritonitis (and not acute appendicitis), independently of gender, appendix length and, WT1 or Bcl2 expression ($p < 0.01$ and $p = 0.02$, respectively).
Conclusion: The results of this study suggest that acute appendicitis occurring in NAP was related to lack of submucosal involvement by the NAP and to WT1 expression. The lack of submucosal involvement in NAP predicted the association of peritonitis-type lesions.

PS-13-058
Epstein Barr virus infection in gastritis with benign lymphoid infiltration
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Objective: The association of Epstein Barr virus (EBV) with gastric malignancies has been proven in many studies in the literature. However, information about EBV associated inflamation/gastritis is remains limited.
Method: 119 gastritis cases with Wotherspoon Grade 2–3 inflammation but without H.Pylori were included the study. Chromogenic in situ hybridization (EBER) and immnunhistochemistry (LMP-1 antibody) were performed. The prevelance of EBV and its relationship with age, intestinal metaplasia and atrophy were analyzed.
Results: 14 cases showed positive staining for EBV. EBV positivity was seen mostly in the lymphoid tissue (13 cases), but it was also detected at the gastric epithelium (7 cases). The mean age of the patients was 44,which is slightly younger than the EBV negative cases (48). Intestinal metaplasia was detected 7 % of the cases. Interestingly, EBV positive cases had higher incidence of atrophy (21 % vs 3.8 % without EBV) .
Conclusion: EBV can be detected in 12 % of the gastritis cases without H. Pylori infection.It is very close to the incidence of EBV associated gastric carcinoma (10 % in the literature). Endoscopic follow-up may be appropriate for gastritis cases which are EBV–positive.

PS-13-060
Evaluation of p53 immunohistochemical expression in high-risk colorectal adenomas
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Objective: Screening for early detection of colorectal malignancies has demonstrated efficacy in reducing disease-specific mortality. Current surveillance guidelines recommend a 3-year follow-up colonoscopy after detection of high-risk adenomas, defined by multiplicity (three or more) or advanced lesions (>1 cm in diameter, villous component and / or high-grade dysplasia). However, this recommendation is exclusively based on endoscopical and histological criteria. Among all the genes related to the adenoma-carcinoma sequence, mutations in TP53 plays an important role. Our objective was to evaluate immunohistochemical expression of p53 in high-risk adenomas of a large cohort of patients, whom underwent surveillance colonoscopy, and to determine its association with recurrence.
Method: A tissue micro-array with 479 adenomas was created and immunostain of p53 (Clone D07, Roche) was performed and analyzed.

Results: Fifty p53-positive cases (10.43 %) were identified: 8 cases (16 %) showed diffuse expression (>90 %), 33 (66 %) partial expression (10–90 %) and 9 (18 %) were focally positive (<10 %). Respect the surveillance colonoscopy, 7/50 positive cases (14 %) were associated with high-risk adenomas recurrence.
Conclusion: We have demonstrated 10.43 % of p53 positivity in a large series of high-risk adenomas. Further studies are in process, including molecular analysis of TP53, in order to rule out other associations with the findings in the surveillance colonoscopy.

PS-13-061
Expression of GRP78 protein is increased in rectal adenocarcinoma
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Objective: Due to tumour chemoresistance, preoperative chemoradiation often partially shrinks rectal adenocarcinoma without complete eradication. The underlying mechanisms of cancer chemoresistance are not clear. GRP78 is an endoplasmic reticulum chaperone protein critical for protein quality control, which might be associated with cancer chemoresistance. The study aims to explore whether the expression of GRP78 protein in rectal cancer is increased compared to the normal colonic epithelium and further upregulated in residual tumour following chemoradiation.
Method: The expression of GRP78 was assessed in normal rectal mucosa and adenocarcinoma by immunohistochemistry. Immunostaining intensity of GRP78 protein was categorized as no or weak staining (0–1+) and strong staining (2–3+). Fisher's exact test with two tails was performed for statistical analysis.
Results: There is minimal expression of GRP78 protein in normal rectal mucosa. GRP78 expression in rectal adenocarcinoma is markedly upregulated compared with normal rectal mucosal epithelium ($p = 0.001$). Furthermore, Residual cancer cells after chemoradiation show uniform strong cytoplasmic expression of GRP78.
Conclusion: This study shows that the expression level of GRP78 is significantly increased in rectal adenocarcinoma compared to the normal colonic mucosa. Residual adenocarcinoma after chemoradiation has a diffuse strong GRP78 expression pattern. Increased GRP78 expression may contribute poor responsiveness of rectal adenocarcinoma to chemoradiation.

PS-13-062
Can definitive diagnosis of metastasis from colorectal carcinoma be established using SATB2 and/ or CDX2 immunohistochemistry?
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Objective: CDX2 is routinely used for identifying gastrointestinal origin of metastatic adenocarcinomas; but a high percentage of other carcinomas also show positivity with this antibody. SATB2 is a new immunohistochemical marker with a few scientific studies showing that it is specifically expressed in a large majority of colorectal carcinomas. This study was proposed to compare SATB2 with CDX2.
Method: The retrospective study included 67 liver biopsies, 108 lymph nodes in resections and 36 serous effusions. Sections stained for SATB2 and CDX2 were assessed individually by two pathologists.
Results: Sensitivity for CDX2 in cases of metastasis from colorectal adenocarcinomas for two pathologists was 93 % and 89 %; while specificity was 72 and 70 %. Similarly sensitivity for SATB2 was 74 and 77 %; while specificity was 72 and 78 %. Kappa value for two pathologists in case of CDX2 and SATB2 was 0.49 and 0.68 respectively for metastasis from colorectal adenocarcinomas and 0.60 and 0.53 respectively for metastasis from non-colorectal adenocarcinomas.
Conclusion: CDX2 is still a more sensitive marker compared to SATB2 for detecting metastasis from colorectal adenocarcinoma; while the specificity of both markers is almost same. SATB2 can be used as a supplementary marker along with CDX2 to identify colon-rectum as the primary site in material from patients presenting with metastasis.

PS-13-063
D2-40 monoclonal antibody and Crohn's Disease: About a series of 15 cases and review of literature
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Objective: The aim of our study is to evaluate lymphangiogenesis by D2-40 expression in Crohn's disease (CD).
Method: Our series is composed of 15 ileo-colonic specimens from patients affected by CD. Three samples of each specimen containing areas of normal intestine wall are formalin-fixed, paraffin-embedded and stained with hematoxyline-eosine . Immunohistochemistry (IHC) using D2-40 monoclonal antibody is then performed. Microscopic study evaluates density of lymphatic vessels, the degree of lymphangiectasy, the situation of lymphoid aggregates, presence of lymphocytic thrombi within lymphatics.
Results: In all specimens ,comparatively with normal intestinal wall , lymphatics are numerous, observed in all layers , dilated with aggregates and granulomas situated very close to the vessel walls. In approximatively half of cases, vessel lumens show total obstruction by lymphocytic thrombi.
Conclusion: Pathogenesis of CD remains unclear even if many hypotheses have been advanced. The role of lymphatics vessels and their possible dysfunction in this chronic disorder has been suggested to explain oedema and inflammation but some authors suggest that lipid deposition could be the primary factor leading to lymphoedema. The presence of lymphocytic thrombi and the preferential situation of aggregates close to wall vessels constitute a morphological aspect few documented in literature.

PS-13-064
4EBP1 expression in colorectal adenomas: Relationship to dysplasia and stem cell phenotype protein CD133
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Objective: 4EBP1 (4E-binding-protein 1) along with 4EBP2 are small proteins that may interfere with translation and with a reversion of a transformed phenotype.
Method: Phosphorylated p4EBP1 expression was studied by immunohistochemistry in colorectal adenomas on tissue microarrays. The expression patterns (cytoplasmic, present/absent) were analyzed with regard to the main morphological features and to CD133, mTOR and PTEN data (Medcalc, rank correlation tests).
Results: Nuclear and cytoplasmic p4EBP1 were correlated (Kendall $p < 0.01$/tau = 0.657). Nuclear p4EBP correlated with decreased adenoma size (Kendall $p = 0.01$/ tau = −0.216), low grade dysplasia (Kendall $p < 0.01$/tau = −0.258) as well as with nuclear PTEN (Kendall $p < 0.01$/tau = 0.369) and, membrane mTOR (Kendall $p < 0.01$/ tau = 0.273). When considering global expression (nuclear or cytoplasmic) p4EBP1 correlated, besides to low grade dysplasia (Kendall $p = 0.04$/tau = −0.179) to the extent of mucosecretion (Kendall $p = 0.02$/tau = 0.206) and to global (cytoplasmic or membrane) CD133 (Kendall $p = 0.05$/tau = 0.196).
Conclusion: The results of our study suggest for the 4EBP1 protein an interference with initial steps of adenomagenesis since correlated decreased tumour size, low grade dysplasia, increased mucosecretion as well as to the stem cell phenotype protein CD133.

PS-13-065

Topography immunohistochemical markers in pancreatic ductal adenocarcinoma: Application of MSH2, MSH6, MLH1

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Objective: Pancreatic cancer is one of the most aggressive and chemoresistant tumour. Tumours of the pancreas as well as colorectal cancer could be associated with MSI. The level of MSI has a proven prognostic value, but its predictor role steel not clear. Tumour cells with a normally functioning repair system could be chemoresistance. We investigated tumours with the positive expression of MMR proteins and give a topography distribution of MSI in ductal pancreatic carcinoma.
Method: We investigated the expression of MSH2, MSH6 and MLH1 in 105 cases of pancreatic ductal carcinoma using TMA technology.
Results: The positive expression (absence MSI) using MSH2, MSH6 and MLH1 in central part of tumour 71,88 , 69 and 74 % of cases respectively. In peripheral areas of the tumour the rate of expression (no loss MMR) of MSH2, MSH6 and MLH1 was lower (68,63 , 62,96 and 69,09 %). But in metastasis positive expression MSH2 and MSH6 was significantly higher (86,36 and 86,21 %)
Conclusion: MSI of all three proteins was low (28–34 %) and comparative in the central part of tumour and periphery and bit lower in metastasis (14–20 %).

PS-13-066

Enteropathy-type T-cell lymphoma associated with diffuse large B-cell lymphoma in celiac disease: A case report

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Objective: We herein present a rare case of enteropathy-type T-cell lymphoma (ETCL) associated with diffuse large B-cell lymphoma (DLBCL) in celiac disease (CD)
Method: A 46 year-old woman with a history of CD presented with impaired general condition. Endoscopic examination suggested a malignant complication. A jejunal resection was performed.
Results: Microscopically, the specimens demonstrated a diffuse lymphomatous proliferation. Immunohistochemistry highlighted two lymphomatous contingents: A lymphomatous contingent of phenotype B CD20 +, CD79a +, PAX5 + with expression for BCL2 and MUM1. A second lymphomatous contingent of CD2 +, CD3 +, CD30 + T phenotype with expression of the cytotoxic markers perforin and granzyme B. The detection of EBV by in situ hybridization using Ebers probes is negative. In molecular biology, there is a monoclonal rearrangement B and a polyclonal profile TCRG and TCRB. Presence of a rearrangement of the MYC gene in favor of a translocation of this gene. These findings are consistent with the diagnosis of enteropathy-type T-cell lymphoma (typeI) associated with diffuse large B-cell lymphoma BCL2 + characterized by a rearrangement of the Myc gene.
Conclusion: ETCL of the small intestine is a well documented complication of celiac disease. Although association with B-cell lymphoma is rare, it should be kept in mind.

PS-13-071

Extracolonic serrated adenomas: The Hungarian Serrated Adenoma Registry (HUSAR) experience

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Objective: Serrated adenomas (SA) are rarer lesions in colon lately gaining more importance along the serrated pathway, but very few data is available about extracolonic SAs.
Method: We diagnosed 2 appendiceal Sessile Serrated Adenomas (SSA) having characteristic serrated, basally dilated crypts - one removed in appendicitis, another beside a villous adenoma in right colon. Another gallbladder was sent with a "stone" inside, which proved to be a 1,5 cm polypoid structure growing out from mucosa, showing all three features of Traditional Serrated Adenomas (TSAs): Ectopic Crypt foci (ECF) and Slit-like serration were dominant, while serrated dysplasia (eosinophylic cytoplasm with centrally located nuclei) was also present.
Results: Appendiceal SSAs are rarely reported and usually side findings, thus we do not know their true prevalence. Our gallbladder TSA is the second such reported lesion, the first reported one was beside a carcinoma in the cholecyst.
Conclusion: Serrated lesions are more common in colon, but do occur extracolonically. Appendiceal, stomach, oesophageal SAs are rearely reported but some studies underlined the higher risk of malignancy of those. Intracolonic serrated lesions gained more attention, but very scarse data is available about extracolonic ones thus we should collect those in a registry to understand/interpret their possible role in carcinogenesis.

PS-13-072

Expression of connexin 43 and connexin 32 in adenomatous polyps and hyperplastic polyps

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Objective: Connexins was thought to be a tumour suppressor gene through normal functioning Gap junctions, but new studies have reported abnormal growth in various carcinomas and sarcomas. Therefore it was aimed to investigate the expression of connexin 43 (Cx43) and connexin 32 (Cx32) in adenomatous and hyperplastic polyps.
Method: This retrospective study included 32 cases with adenomatous polyps and 42 cases with hyperplastic polyps, between 2014 and 2015. 30 of the cases were female and 44 of the cases were male. 11 of the cases were over 50 years old and 63 of the them were under 51 years old. According to the location, there were 50 cases with sigmoid and rectum involvement, while 24 cases had other organ involvements. The lesions were 5 mm or smaller in diameter in 51 cases and 6 mm and larger in 23 cases. Three micron sections were prepared from the existing paraffin blocks and stained with immunohistochemical staining method with Cx43 and Cx32. The preparations were evaluated under light microscope and graded as no staining, weak, medium, severe.
Results: Cx43 and Cx32 staining results changed according to polyp type ($P = 0.039$, $P = 0{,}048$ respectively). Statistically, there were no significant correlations between age, sex, location and diameter with staining pattern.
Conclusion: Loss of Cx43 and Cx32 staining in adenomatous polyps was noted and thought to be related to dysplasia.

PS-13-073

Retrospective revision of V600E BRAF mutated colorectal adenocarcinomas: Clinico-morphological features and re-diagnosis of a series of 10 patients

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Objective: To review the clinico-pathological features of V600E BRAF mutated colorectal carcinomas and to determine if they meet criteria of serrated adenocarcinomas (SAC) applying the recently published criteria for this morphological subtype and reclassify them if necessary.
Method: All BRAF mutated colorectal adenocarcinomas collected at our institution during the last 30 months have been considered ($n = 10$). BRAF

mutations have been analyzed by real-time PCR (Idylla® or Cobas®). Slides have been reviewed by three gastrointestinal pathologists.
Results: Clinically equal sex distribution was observed and the age ranged from 53 to 90 yo, and half of them were asymptomatic (discovered in a screening program or follow up for others diseases) Most of the cases were located on the ascending colon (6/10), and seven out of ten presented in advanced stages III and IV. Histologically, 3 out of 10 cases were diagnosed initially as SAC, two as mucinous AC and 5 as conventional adenocarcinomas (CAC). After review, the pathologists agreed reclassify eight cases as SAC, one case as conventional adenocarcinoma and another as mucinous AC. Only two cases showed loss of DNA repair proteins MLH1 and PMS2 detected by immunohistochemistry.
Conclusion: BRAF mutated adenocarcinomas are a molecular subtype of colorectal tumours related to two pathological subtypes, SAC and CAC. BRAF mutations are more prevalent in SAC than in conventional subtype. Accurate histological diagnosis of SAC is of clinical importance.

PS-13-074
Case report: Gangliocytic paraganglioma
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Objective: Gangliocytic paragangliomas are rare. First described by Dahl in 1985. Kepes and Zacharias introduced the term "gangliocytic paraganglioma" in 1971, because of features similar to ganglioneuroma and paraganglioma. These neoplasms are composed of an admixture of three cell types: epithelioid, spindle and ganglion cells. This tumour has generally been regarded as benign, but a few cases with regional lymph node metastasis and even distant metastasis have been reported.
Method: A 57-year-old woman presented to our institute with dyspepsia. An intraluminal mass at the second portion of the duodenum was discovered in upper endoscopy. The patient underwent endoscopic resection for which pathologic examination of the specimen demonstrated safe margins.
Results: Histological examination showed a circumscribed submucosal mass with spindle cells arranged in nests and trabeculae. Rare ganglion cells were identified, scattered within the spindle cell compartment. The epithelioid cells were positive for chromogranin and synaptophysin. Ganglion-like cells showed positive reactivity for synaptophysin. The spindle-shaped cells showed positive reactivity for S-100 protein. The expression of Ki-67 was <2 %.
Conclusion: In cases in which the tumour is resected with negative margins, it appears to be safe to continue with surveillance and forego adjuvant therapy.

PS-13-076
Signet ring carcinoma of duodenum and cliac disease: Rare coexistence
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Objective: INTRODUCTION: Signet ring carcinoma of duodenum is very rare tumour and its association with celiac disease was reported only ones in scientific literature.
Method: CASE REPORT: Here we report case of 65 year old female patiente with stomach pain, vomit, weight loss, reduction of appetite and jaundice. She was biopsied with clinical diagnosis of pylorus stenosis and signet ring cell carcinoma was found. CT showed the thickening of duodenum wall from bulbus region to Treitz ligament. Gross disection (Whipple o.p) showed mucosal thickening 12 cm in length, 4 cm distal from pylorus (pT4N2MxR1). On histopathological slides we confirmed signet ring cell carcinoma of duodenum, as well as surrounding celiac disease.
Results: In retrospect, we determined that the patiente was suffering from nonspecific stomach pains for 9 years, and that preveously preformed biopsy od stomach and duodenum showed the picture of active gastritis and IBD, so she was never on gluten-free diet.
Conclusion: Although possible connection between celiac disease and signet ring cell carcinoma was never proven it leaves question open:Would untreated celiac disease has led to carcinoma ? Misdiagnosed celiac disease as IBD, ones again, alert us that presence of neutrophilic granulocytes does not excludes celiac disease.

PS-13-078
Tissue-based in situ detection of the clarithromycin resistance for the personalised Helicobacter pylori eradication therapy
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Objective: Clarithromycin-resistance (Cla-res) is the leading cause of treatment failure of Helicobacter pylori (HP) infections. Our aim was to examine the prevalence of clarithromycin-resistant HP-infection and its connection to gender and age in a monocentric cohort.
Method: 4744 HP-positive adults were examined (2708 females; 57.1 %, 2036 males; 42.9 %). HP-positive gastric mucosal tissue slides were investigated by a bacterial rRNA-targeted FISH-test (BactFISH Helicobacter Combi Kit) detecting the clarithromycin-sensitive and -resistant HP-bacteria. HP eradication-related and -independent antibiotic consumption anamneses of these patients were collected in cooperation with the Hungarian National Health Insurance Fund.
Results: Overall Cla-res rate was 17.2 %. Females showed significantly ($p < 0.0001$) higher Cla-res rate (19.8 %) than males (13.7 %). Low Cla-res prevalence (12.9 %) was found in the age group 70+. Cla-res rate reached 20 % in females aged under 70, while it was less than 15 % in males except ages 30–39 (15.3 %). Cla-res prevalence was significantly lower (5.52 %) in macrolide-naive patients than in the macrolide-treated group (30.5 %; $p < 0.001$). No significant difference was found between macrolide-naive females and males (6.4 % vs. 4.6 %; $p = 0.057$).
Conclusion: Gender and age distribution of clarithromycin-resistance should be considered for HP-eradication treatments. Our results suggest that higher prevalence of clarithromycin-resistance in females is related to increased exposition to macrolide antibiotics.

PS-13-080
Downstream applications of purified cell populations isolated from formalin-fixed paraffin-embedded tissue
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Objective: Formalin-fixed paraffin-embedded (FFPE) tissue sections are composed of a variety of cell types, thus introducing tissue heterogeneity bias in downstream applications. We minimized this bias by dissociating FFPE tissue and purifying distinct cell populations. Furthermore, we demonstrate compatibility with downstream applications for DNA and RNA analysis.
Method: A protocol was established by testing different methods for enzymatic and mechanic tissue dissociation of colorectal cancer FFPE tissue, antibody labeling, and cell sorting. Tissue sections were deparaffinized, dissociated with collagenase/dispase solution, labeled with Cytokeratin (CK) and Vimentin (Vim) and sorted by fluorescence-activated cell sorting. Purified populations (CK+/VIM-, CK-/VIM+ and

CK+/VIM+) were used for DNA and RNA extraction and downstream analysis.
Results: DNA analysis of isolated cell fractions confirmed that all isolated populations were 99 % pure, despite differences in tissue composition. RNA expression analysis using NanoString reveals several significantly dysregulated genes ($p < 0.05$).
Conclusion: We demonstrate that purified cell populations can be successfully isolated from FFPE tissue, and that both DNA and RNA can be extracted in sufficient amounts and quality for downstream applications. This method therefore provides a basis for reliable analysis of RNA molecules present in multiple cell types within a tumour, or gradual changes in expression levels, previously missed due to tissue heterogeneity.

PS-13-081
Synchronous and metachronous colorectal cancers: DNA mismatch protein expression and clinicopathological implications of 44 cases
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Objective: Multiple primary tumours accounts for 3–8 % of colorectal carcinomas (CRCs). We investigated the clinicopathological characteristics and DNA mismatch repair protein (MMR) expression of synchronous/metachronous CRCs.
Method: Records of 1128 cases diagnosed between 2002 and 2011 years were reevaluated for presence of synchronous (more than one primary CRC diagnosed within 6 months of resection) and metachronous CRCs (occuring later than 6 months). MMR expression was evaluated immunhistochemically and correlated with nonparametric tests.
Results: Among 44 cases with multiple CRCs, 81 % had synchronous; 18 % had metachronous tumours. The median age was 69 ± 13.3 (range:35–91) vs 68.5 ± 8.2 (range 54–79) years-old; female/male ratio was 0.16 vs 0.33; most common initial-tumour localisation and pathological stage was left colon (55.6 % vs 75 %); pT3 (77.8 % vs 87.5 %) and pN0 (44.4 % vs 62.5 %) respectively for synchronous and metachronous tumours. Lymphovascular invasion (LVI) (27.5 % vs 0 %), satellite nodule (16.7 % vs. 12.5 %), tumour-infiltrating lymphocytes (TILs) (22.2 % vs 0 %) and expansive tumour border(22.2 % vs 12.5 %) were more frequent in synchronous than metachronous CRCs (statistical insignificant). MMR deficiency was detected 22.2 % of synchronous vs. 12.5 % of metachronous tumours, PMS2-loss being the most frequent (13.6 %), followed by MSH2 (9.1 %), MSH6 (6.8 %); and MLH (2.3 %). PMS2 or MLH1 loss wasn't observed in metachronous tumours.
Conclusion: Synchronous/metachronous tumours accounts for 3.9 % of CRCs in our series. More frequent LVI, satellite nodules, TILs, expansive tumour border and MMR deficiency (particularly MLH1-PMS2) in synchronous CRCs deserves further investigation.

PS-13-082
A marker panel consisting of LC3B, TRIM24 and Caveolin-1 predicts survival of oesophageal adenocarcinoma patients
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Objective: Expression patterns of the autophagy marker (LC3B) have been previously shown b to be associated with survival in oesophageal adenocarcinoma patients. In this study, we have investigated the combined expression of LC3B, TRIM24 and Caveolin-1 as a predictive marker panel of patient outcome in oesophageal adenocarcinoma.
Method: We performed immunohistochemical staining of LC3B, TRIM24 and Caveolin-1 on tumour tissue arrays of 84 chemo naïve oesophageal adenocarcinoma patients.
Results: LC3B cytoplasmic reactivity is associated with tumour differentiation, lymph node metastasis, tumour pathological stage and neural invasion. LC3B globular structures are only associated with lymph node metastasis and tumour pathological stage. There is a correlation between Caveolin-1 expression either in tumour cells or tumour stromal cell and tumour pathological stage and lymphatic metastasis. Each marker (LC3B, TRIM24 and Caveolin -1) predicts overall survival on univariate analysis. Positive for LC3B globular structures, TRIM24 expression and Caveolin-1 expression in tumour cells are associated with poor prognosis ($p = 0.001$, $p = 0.012$ and $p = 0.005$ respectively). While positive LC3B cytoplasmic expression and Caveolin-1 expression in tumour stromnal cells are associated with better prognosis ($p = 0.001$ and $p = 0.005$, respectively). Using a combined panel of the three markers increases the statistical significance (p-value) to < 0.000. On multivariate analysis, the markers panel is an independent prognostic factor for overall survival ($p = 0.005$) when adjusted for other independent predictors of outcomes.
Conclusion: We have identified a panel of three markers; LC3B, TRIM24 and Caveolin-1 that correlates with patient outcome in oesophageal adenocarcinoma.

PS-13-083
The association of GSTT1 and GSTM1 genes polymorphism and the risk of colorectal cancer - the preliminary results
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Objective: Glutathione S-transferase (GST) gene polymorphism is known to be associated with body antioxidant and detoxification capacity and therefore could have an impact on colorectal cancer development. The aim of the study was to determine association between GSTT1 I GSTM1 genotype and frequency of colorectal cancer.
Method: Individuals were divided into a case group with a diagnosis of colorectal cancer and control group without the disease based on colonoscopy and histopatology results. DNA was extracted from peripherial blood samples. GSTM1 and GSTT1 genotypes were determined by using qPCR method with the Taqman probes.
Results: So far a total of 153 (80 patients and 73 controls) were genotyped for the deletion polymorphism of two GST isoforms. There were no statisticaly significant differences in GSTM1-null or GSTT1-null frequency between these two groups. Moreover there was no difference in combined frequencies of GSTM1and GSTT1 polymorphisms between patients and control.
Conclusion: The results did not find any association between GSTM1 and GSTT1 polymorphisms and colorectal cancer susceptibility. There is no association between the combination of GSTM1 and GSTT1 polymorphisms and risk of this malignancy also. However the preliminary results need to be confirmed in a larger cohort.

PS-13-085
A digital pathology-based mass spectrometry approach to biomarker discovery in formalin-fixed paraffin-embedded colorectal cancer tissue
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Objective: The current TNM staging system suboptimally reflects survival in colorectal cancer patients. We therefore aim to identify novel prognostic biomarkers in stage II and III CRC patients using selectively isolated formalin-fixed paraffin-embedded (FFPE) cell populations with a shotgun-proteomics based approach.

Method: Cell populations were isolated by annotating regions of interest on a digital histological scan of CRC tissue from stage II and III patients. Annotated scans were aligned with the tissue block, and precise regions of interest were punched out using a tissue microarray tool. Punched cores were re-embedded into a new block, and used for protein extraction and mass spectrometry analysis.
Results: Our findings indicate reliable identification and quantification of hundreds of proteins from FFPE tissue (intra-class correlation for reproducibility: 0.982). Volcano plot analysis identified 20 significant (adjusted $p < 0.05$) biomarkers in epithelial cell populations in stage II and III CRC. Several of these have been linked to cancer in previous studies, including PPA1, CSTB, TXN, ALDH1B1 and PARK7.
Conclusion: Our data suggest that we can successfully analyze specific populations of cells from FFPE tissue on the protein level using mass spectrometry. Our method quantitatively identified several previously unreported biomarkers, possibly rendering it superior to immunohistochemical approaches.

PS-13-086
Shotgun proteomics-based mass spectrometry analysis of purified cell populations isolated from fresh colorectal cancer tissue
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Objective: We demonstrate that tissue heterogeneity in fresh colorectal cancer tissue can be minimized by isolating and purifying selected cell populations, thus circumventing potential bias for subsequent tissue analysis.
Method: Fresh normal and tumour colon tissue was dissociated into single cells. Cells were labelled with EpCAM followed by mild fixation in formalin to prevent sample deterioration. Samples were then subjected to fluorescence-activated cell sorting (FACS), and the purified EpCAM+ population was used for mass spectrometry analysis. An identical analysis was performed with the Colo205 cell line for comparison.
Results: FACS reveals consistent high yields (>1 million EpCAM+ Cells) isolated from fresh tissue. SDS-PAGE of protein extracts from fresh tissue isolated and Colo205 cells reveals very similar protein quantity and size distributions. Additionally, mass spectrometric analysis of 1 million purified EpCAM+ cells reveals 2197 proteins identified across all major subcellular compartments.
Conclusion: We show that EpCAM+ cells can be successfully purified from fresh tissue and used for mass spectrometric analysis. Protein profiles of EpCAM+ purified cells are almost identical to those of Colo205 cells, confirming their epithelial origin. Our mass spectrometry results further indicate that protein identifications contain no bias towards any specific subcellular localisation.

PS-13-087
Adenoviral infection in a series of 25 adult small-bowel transplants
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Objective: Adenoviral infection (ADVI) ranges from a mild (respiratory, gastrointestinal, ocular) to a severe disseminated disease. In adult small-bowel transplants (SBT), there are very few described cases.
Method: We identified 4 episodes (3 patients) of ADVI in the intestinal graft biopsies (typical epithelial nuclear inclusions) among 25 SBT in 23 adult patients (2004–2017)
Results: 1) A 45-year-old man (4220 days of SBT) suffered ADVI on days 55–60. As crypt apoptoses increased, moderated acute cellular rejection (ACR) was also diagnosed. Episode resolved with steroids and Campath-1H. A new ADVI was noticed (day 154–189) in biopsies without other signs. He didn't require treatment. 2) A 30-year-old woman (460 days) with mild ACR (on day49: steroids) suffered (on day67) a profuse ostomy output and ADVI was seen during 38 days (without crypt apoptoses). She recovered in a few days after cidofovir and decrease of immunosuppression. 3) A 62-year-old woman with severe ACR (day7–63: Campath-1H) died of sepsis (day81). ADVI was seen just before dying.
Conclusion: A) ADVI was frequent and occurred within the first 6 months after SBT. B) Immunotherapy for ACR preceded ADVI in 2 of 4 episodes. C) ADVI may not be symptomatic. Biopsies of ADVI with crypt apoptoses can mimic ACR.

PS-13-088
Alterations of interstitial cells of Cajal (ICC) in the rat colon in diabetes
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Objective: Interstitial cells of Cajal (ICC) are mesenchimal cells inserted between neurons and smooth muscle cells of the gastrointestinal tract. Certain ICC subtypes serve as source of electrical slow waves which are electrophysiological foundation of peristalsis, while other ICC subtypes are mediators and modulators of enteric motor neurotransmission, mechanoreceptors. ICC disorders caused by metabolic changes in diabetes could explain symptoms of diabetic gastroenteropathy (gastroparesis, slow intestinal transit, constipation, diarrhea, fecal incontinence, abdominal pain). The objective of the present study is to determine the ICC distribution and morphology in colon of rats with streptozotocin-nicotinamide induced diabetes mellitus using immunohistochemical and morphometric methods.
Method: Material and methods: The material consisted of 12 rat proximal and distal colon dissections (diabetic group and control group; $n = 6$ per group). Immunohistochemical examination was performed by kit-polymer detection (C-kit).
Results: In both proximal and distal colon of diabetic rats, intramuscular ICC were very rarely present and linear cell-cell connections between these cells were completely missing. Also there was decrease in myenteric ICC. There were no significant alterations in submucosal ICC distribution.
Conclusion: Decrease of intramuscular ICC and myenteric ICC was observed in colon in diabetes, but without submucosal ICC alterations. Loss of ICC networks may play a major role in peristalsis disturbance.

PS-13-089
Interobserver agreement in the diagnosis of inflammatory bowel disease-associated dysplasia: A multicenter study of 125 cases
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Objective: Dysplasia diagnosis in long-standing inflammatory bowel disease (IBD) surveillance biopsies have shown low or moderate interobserver agreement. Or aim is to evaluate the reproducibility of the current classification in a multicenter Spanish study as first step to study miRNA expression in IBD associated dysplasia.
Method: A total of 125 biopsies were selected. Eight pathologists blinded to each other classified the samples into normal mucosa, inflammatory, reactive changes, indefinite, low grade, high grade dysplasia and adenocarcinoma. Global and paired interobserver agreement were calculated with weighted k and intraclass correlation coefficients (ICC), and defined as fair: 0,21–0,40; moderate: 0,41–0,60; good: 0,61–0,80 and very good: 0,81–1,00. We also analyzed the concordance in two different groups: experts and non experts.
Results: Global agreement calculated with ICC was 0,776 ($p < 0,001$). The interobserver agreement by pairs was good or very good for all the observers with a weighted k ranging from 0,69 to 0,87 ($p < 0,001$). There

was good agreement among the non-expert group: ICC 0,75 ($p < 0,001$) and very good among the expert group: ICC 0,85 ($p < 0,001$).
Conclusion: This study reveals higher interobserver agreement on the interpretation of colonic dysplasia in IBD than other already published. We think this may be due to the weighted calculation of the concordance, which gives greater meaning to more significant differences between the diagnostic categories.

PS-13-090
AKT inhibition is an effective treatment strategy in ARID1A-deficient gastric cancer cells
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Objective: We aimed to investigate the different sensitivity for the AKT inhibitor in ARID1A-deficient gastric cancer (GC) cells.
Method: After transfection using siRNA or shRNA, the effect of ARID1A knockdown on the PI3K/AKT signalling pathway was evaluated by Western blot analysis. ARID1A-knockdown cells were treated with AKT inhibitor (GSK690693), 5-fluorouracil, or cisplatin alone or in combination. Viability and apoptosis were analyzed using EZ-CYTOX cell viability assay and flow cytometry, respectively.
Results: ARID1A depletion accelerated the phosphorylation of AKT and S6 downstream proteins in a dose-dependent manner, and led to an increased proliferation of MKN-1, MKN28, and KATO-III GC cells ($P < 0.001$). ARID1A-deficient cells were more vulnerable to the GSK690693 ($P < 0.001$), even at very low doses. Flow cytometry confirmed the increased apoptosis in ARID1A-deficient cells treated with GSK690693 (0.01 μmol/L) ($P < 0.001$). In contrast to our expectations, ARID1A-depletion did not cause resistance to 5-fluorouracil or cisplatin. Addition of GSK690693 to the conventional chemotherapy induced more decreased cell viability in ARID1A-knockdown cells ($P < 0.01$).
Conclusion: Loss of ARID1A expression is a surrogate marker for the activation of the AKT signaling pathway and is also a reliable biomarker to predict the response for the AKT inhibitor.

PS-13-091
HER2 status in gastric carcinomas with prevalent cribriform component
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Objective: Although a peculiar cribriform histopathological pattern has not been described in the last WHO classification of gastrointestinal tract tumours, in gastric carcinomas (GC) a cribriform component (CGC) has been rarely identified. The aim of the present study is to analyze the HER2 status in a cohort of CGC, in comparison to classic GC, in order to evaluate the possible relationship with clinic-pathological characteristics as well as prognostic parameters.
Method: In thirty-seven formalin-fixed paraffin-embedded tissue (CGC) blocks the HER2 status has been evaluated using HercepTest (DAKO). All cases considered equivocal (2+) have been further assessed by FISH test (pharmDx DAKO).
Results: The tumours were taken from 19 men and 18 women (mean age 68 years; range 40–84 years). The overall HER2 amplification in CGC was encountered in 8/37 cases (21.62 %); in detail, 6/37 (16.22 %) were scored as 3+, 4/37 appeared equivocal with 2+ score, two of which showed FISH amplification. Finally, 3/37 (8.10 %) were 1+ and 24/37 (64.86 %) were categorized as 0.
Conclusion: The higher rate of HER2 amplification in CGC further confirms the aggressive behaviour of this GC variant also documented by other unfavourable parameter such as lympho-vascular invasion, higher stage and lower disease free-survival in comparison to conventional GC.

PS-13-092
Neuroendocrine differentiation in early gastric carcinomas-correlation with clinical, morphological features and adequacy of endoscopic submucosal resection
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Objective: An expression of neuroendocrine (NE) markers in 61 cases of early gastric cancer (EGC) removed by endoscopic submucosal dissection (ESD) was correlated with clinical, histopathological features and resection adequacy rates to determine if NE differentiation indicates a potentially more aggressive behaviour of early stage GC.
Method: To evaluate the pattern of NE proliferation, percentage of NE elements within tumours and neuroendocrine hyperplasia in adjacent mucosa, an immunohistochemical staining for chromogranin (CgA) and synaptophysin (Syn) was performed and evaluated semiquantitatively.
Results: Immunohistochemical expression of NE markers was observed in 29/61 (47.5 %) of examined EGCs. 7/61 (11.5 %) EGCs showed positivity of NE markers in more than 30 % of cells. NE hyperplasia in benign gastric mucosa in the vicinity of the tumour was significantly more common in EGCs with NE differentiation (EGC NE+).
Conclusion: Our study showed NE differentiation in approximately half of the examined EGCs. The presence of more than 30 % of NE positive cells is not a sufficient to classify GCs as MANECs especially when tumours did not demonstrate morphological features of NE differentiation, higher histologic grade or lower complete resection rates. Further studies in larger groups are necessary to better define the significance of NE differentiation in EGC.

PS-13-093
Poorly differentiated cluster in colorectal adenocarcinomas shares biological similarities with a micropapillary pattern as well as tumour budding
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Objective: In colorectal carcinoma, poorly differentiated cluster (PDC) is a poor prognostic indicator showing morphological continuity and behavioral similarities to tumour budding (TB) and a micropapillary pattern (MPP). However, the pathogenesis of PDC has not been well investigated.
Method: To clarify the biologic nature of PDC, we compared the expression patterns of β-catenin, E-cadherin, EpCAM, Ki-67, MUC-1, and EMA in PDCs, TB, and differentiated neoplastic glands of the tumour center (TC).
Results: In the study group (117 cases), indices of nuclear β-catenin were higher in PDCs (37.3 %) and TB (43.3 %) than in TC (8.9 %, $p < 0.001$). E-cadherin and EpCAM showed a tendency of being preserved along the cell membrane in TC (91.5 and 92.3 %, respectively) whereas they were lost in PDCs (44.4 and 36.8 %, respectively) and TB (60.7 and 68.4 %, respectively). The mean Ki-67 labeling index in TC was 71.5 %, whereas it was decreased in PDCs (31.2 %) and TB (10.2 %, $p < 0.001$). An inside-out pattern for MUC1 and EMA was frequently observed in PDCs (48.7 and 45.3 %, respectively) and TB (46.2 and 45.3 %, respectively) but not in TC.
Conclusion: Our findings suggest PDC is linked to epithelial-mesenchymal transition and there is a pathogenetic overlap or the same phenomenon among PDC, TB, and MPP.

PS-13-094

Investigation of GST isoenzymes, multidrug resistance proteins and apoptototic effect in DLD-1 human colon cancer cell line before and after 5-fluorouracil treatment

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Objective: Cancer cells that develop resistance to chemotherapeutic agents are a major clinical obstacle in the successful treatment of cancer. Glutathione S-transferases (GSTs) play an important role in the response of tumours to chemotherapy. ATP dependent transporters are involved in drug resistance in a similar manner to the drug transporter in multidrug resistance (MDR) of human colon cancer cell line.
Method: In this study, immunocytochemical expressions of MDR-1 (P-gp), MRP1, 2, 3, 6 and 7, GSTA-1, GSTM1, GSTT1, GSTP1, GSTO1, GSTZ1, GSTS1, and GSTK1 were examined in DLD-1 human colon cancer cell line before and after 5-fluorouracil (5-FU) treatment. Medium containing 5-FU was changed every 3 days. After incubation, colonies were washed in PBS, fixed with methanol for 15 min and washed in PBS. The harvested colon cells were immunostained. Treated and untreated cancer cells were scored according to their immunostaining intensity.
Results: The GSTP1, GSTT1, GSTM1, GSTA1, GSTO1, GSTZ1 and GSTK1 expressions were higher in treated colon cancer cells than those in untreated DLD-1 human colon cancer cells. Similarly, the MRP2, MRP 3, MRP6 and MRP7 expressions were higher in treated colon cancer cells than that in untreated DLD-1 human colon cancer cells. However, there was no statistical difference in GSTS1, MDR1, and MRP1 expressions.
Conclusion: GSTP1, GSTT1, GSTM1, GSTA1, GSTO1, GSTZ1, GSTK1 and MRPs might be important in inactivating 5-fluorouracil in this treatment with and drug resistance in colon cancer.

PS-13-095

Tumour deposits as a marker of colorectal cancer progression: Frequency and correlation with primary tumour stage

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Objective: Our study aimed to reveal tumour deposit (TD) frequency in patients with colorectal cancer (CRC) and determine a correlation between this phenomenon of disease progression and primary tumour stage.
Method: We conducted a retrospective study and analyzed histological data from surgical specimens of 209 patients with verified CRC. All patients underwent radical surgical treatment with expanded D3-lymphodissection.
Results: In the analyzed specimens, the average number of the lymph nodes (LNs) was 21.4 ± 0.8. There were TDs in mesocolic tissue among all histological specimens of 68 patients (32.5 %). We observed TDs in 15 from 20 samples (75 %) for pT4b tumours, in 5 from 9 samples (55.6 %) for pT4a tumours, and in 47 from 138 samples (34.1 %) for pT3. For tumour pT2 TDs were revealed only in one case among 38 patients (2.7 %). When no LNs were involved (n = 109), we found TDs in 10.1 % of specimens (n = 11). When the first-order LNs were involved (paracolic LNs) (n = 62), 50 % of patients had TDs; and when the second-order LNs were involved (n = 32), 71 % of patients had them. We observed TDs in all specimens of patients (n = 3) with lesion of the first-, second-, and third-order LNs (paraaortic LNs). We found TDs in 56 % of patients with stage IV CRC (n = 30) and in 59 % of patients with stage III CRC (n = 84).
Conclusion: Thus, TDs are a marker of CRC progression, and their frequency depends on disease stage, depth of primary tumour invasion, and LN lesion.

PS-13-097

Aberrant TTF-1 expression in colorectal carcinomas: An immunohistochemical analysis of 1,319 cases using three different antibody clones

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Objective: The aim of this study is to investigate the frequency of aberrant expression of thyroid transcription factor-1 (TTF-1), a specific marker of thyroid or lung tissue, in colorectal carcinomas (CRCs) and its clinicopathological and molecular associations.
Method: Immunohistochemistry for TTF-1 using three different antibody clones (8G7G3/1, SPT24, and SP141) was performed on tissue microarray sections of 1,319 primary CRCs.
Results: Among the 1,319 CRCs, TTF-1 expression was detected in 66 cases by both the clones SPT24 and SP141, and it was detected in 2 cases only by the clone SP141. TTF-1 expression was not detected in any cases when the clone 8G7G3/1 was used. The 66 CRCs with TTF-1 expression detected by both SPT24 and SP141 were considered as TTF-1 positive cases in this study. TTF-1 positivity was significantly associated with distal tumour location, non-mucinous histology, intact CDX2 expression, CpG island methylator phenotype-negative status, microsatellite-stable status, and low frequency of KRAS mutations in CRCs.
Conclusion: Our study confirmed that the frequency and characteristics of aberrant TTF-1 expression in CRCs vary depending on the antibody clone. TTF-1 immunohistochemistry using the clone SPT24 or SP141 should be performed cautiously when identifying the organ of origin of metastatic carcinoma.

PS-13-098

A somatic TP53 mutation in combined low grade appendicular mucinous neoplasm and carcinoma ex-goblet cell carcinoid suggesting a common origin for both neoplasms

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Objective: To report a combined low grade appendicular mucinous neoplasm (LAMN) and carcinoma ex-goblet cell carcinoid (CEGCC) with Next Generation Sequencing (NGS) analysis.
Method: A 60-year-old male with peritoneal carcinomatosis was submitted to cytoreductive surgery with hyperthermic intraperitoneal chemotherapy.
Results: An incidental LAMN up to the appendicular submucosa (pT1N0, AJCC/UICC 7th) was admixed with an advanced CEGCC (pT4N1M1) type C of Tang et al (high grade neuroendocrine carcinoma with residual goblet/signet ring cells). LAMN and CEGCC shared immunophenotype (CK7, CK20, MUC2, CDX2, CK19, MUC5ac) being only CEGCC positive for synaptophysin and chromogranin. Targeted-NGS was performed in CEGCC, LAMN and non-tumoural paraffin embedded samples using Trusight Tumour 26 Panel (Illumina, San Diego,CA). Results were analyzed using Variant Studio 2.2 and Integrative Genomics Viewer 2.3 software. A missense TP53 Y220C mutation located in exon 6 was detected in both CEGCC and LAMN and absent in non-tumoural sample. Non-pathogenic synonymous variants were also found in APC, KIT, KRAS, MET, PDGFRA and TP53.
Conclusion: In this case, the association of CEGCC with LAMN showing identical somatic TP53 mutation doesn't support a collision tumour. Instead, a common origin derived from a pluripotential cell with the ability of divergent mucinous and neuroendocrine differentiation is proposed.

PS-13-099

The influence of radiotherapy on normal rectal wall in rectal carcinoma - morphometric study

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Objective: The authors compared the mean thicknesses (MT) of rectal wall layers in the neighborhood of carcinomatous tumours in two distinct groups, divided by the presence of preoperative irradiation.
Method: The studied material consisted of cross sections of the proximal lateral and distal rectal wall in the vicinity of 34 non-irradiated and 25 irradiated tumours, fixed in buffered formalin, included in paraffin, and stained with hematoxylin eosin. The mean thicknesses of main rectal wall layers (mucosa-M, submucosa-SM and tunica muscularis-TM) were determined in three points mentioned above (proximally, distally and laterally to the tumour) with dedicated image analysis software.
Results: Rectal mucosa MT presented no significant differences between the two groups in all three determination points. In turn, SM and TM around the irradiated tumours had usually a greater MT than SM and TM around the non-irradiated tumours in all three determination points caused by the presence of an obvious fibrosis process who was replacing the normal structures of these layers.
Conclusion: Rectal wall undergoes a remodeling process influenced by the preoperative irradiation consisting in the development of fibrosis located mainly in the SM and TM layers. Further studies on larger series are required to validate these observations.

PS-13-100

Prognostic signification of Goseki classification in gastric adenocarcinoma

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Objective: The aim of the study was to determine impact of Goseki classification on overal survival time.
Method: The study included 96 patients with gastric adenocarcinoma who had a radical gastric surgery.
Results: Avarage follow-up period of patients was 27 ± 17,4 months. According to Goseki classification they was grouped into categories: I - well differentiated, poor with mucus (40.6 %); II - well differentiated, rich with mucus (13.5 %); III - bad differentiated, poor with mucus (30.2 %); IV - bad differentiated, rich with mucus (15.6 %). We found longer survival time of patients with Goseki type I compared to patients with Goseki type II, but the difference was not statistically significant (Log Rank test = 3.749, $p = 0.053$). Survival time of patients with Goseki type I was significantly longer than patients with Goseki type III (Log rank test = 5.709, $p < 0.05$) and Goseki type IV (Log rank test = 5.009, $p < 0.05$). Survival time of patients with Goseki type II was not significantly longer than patients with Goseki type III and Goseki type IV. Survival time of patients with Goseki type III was not significantly longer than patients with Goseki type IV.
Conclusion: Goseki classification were not significant prognostic parameters in patients with gastric adenocarcinoma.

PS-13-101

Mucinous epithelial tumours of the appendix: A clinicopathological study of 50 cases

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Objective: The classification of mucinous epithelial tumours of the appendix (META) has been the source of considerable controversy. Our aim is to review a case series of META using the most recent diagnostic criteria of the WHO classification and to evaluate their clinicopathological features.
Method: Fifty cases of META diagnosed in the department of pathology of the university Hospital of Sfax (Tunisia), were collected from January 2003 to December 2015.
Results: META were classified as adenoma in 48 %, low-grade appendiceal mucinous neoplasm (LAMN) in 42 % and mucinous adenocarcinoma (MC) in 10 %. The Mean age at diagnosis was 52,9 years (range: 12–84) for adenoma, 53 years (range: 9–92) for LAMN and 61.4 years (range:51–80) for MC. There was no sex predilection for adenoma however there was a male predominance in both LAMN (sex ratio = 1.33) and MC (sex ratio = 1.5). Pseudomyxoma peritonei (PP) were associated with one case of LAMN and one case of MC.
Conclusion: The better understanding of the histologic criteria of META is mandatory in order to determine each mucinous neoplasm will probably disseminate to the peritoneal cavity.

PS-13-102

Immunohistochemical diagnostic aspects in c-kit negative (GIST) gastrointestinal stromal tumours

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Objective: GIST are rare mesenchimal tumours that are most commonly diagnosed based on immunohistochemical stain of CD117 which highlights overexpression of kit protein. This study aims to investigate kit negative GIST and to emphasize the diagnosis difficulties in the management of these patients.
Method: From the archives of Fundeni Clinical Institute were identified between January 2004 and July 2016, 140 cases of tumours with histological features of GIST. Clinical (age, gender) , morphological, immunohistochemically and follow up data were analyzed.
Results: The results showed that 11.5 % (16) patients, 5 (31.25 %) women and 11(68.75 %) men with age between 33 and 79 years old (average 60 years old) presented CD117 negative tumours localized in the colon (2), stomach (3) and small intestine (11) . They were confirmed immunohistochemically by PDGFRA, CD34 and DOG1. The microscopic pattern was predominantly fusiform (12 cases) and mixte (4 cases).
Conclusion: Kit negative GIST is a problematic entity which makes diagnostic difficulties. Especially in these cases, DOG1 is a very useful marker and has a higher sensibility and specificity then CD117 . Also in these cases mutational status of KIT and PDGFR can bring lightinto the matter.

PS-13-103

Prognostic significance of the Lauren and Ming classification in gastric adenocarcinoma

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Objective: Data about the importance currently recognized classification of histological type of gastric adenocarcinoma in the prognosis of patients with gastric cancer, are mostly controversial.
Method: Our study included 96 patients with gastric adenocarcinoma who had a gastrectomy. Avarage follow-up period of patients was 27 ± 17,4 months.
Results: According to the Lauren classification, patients were classified as follows: diffuse type—34.4 %, intestinal type—54.2 % and mixed type—11.4 %. Infiltrative tumour margins were present in 94.8 % of patients and expansive in 5.2 %. Statistically significant better survival was found in patients with expansive type of tumour margins compared to the infiltrative type (Log Rank test = 6.266, $p < 0.01$). Statistically significant better

survival was found in patients with intestinal type than in patients with mixed type (Log Rank test = 5.913, $p < 0.01$), while there was no statistically significant difference in survival of patients with intestinal type than of patients with diffuse type ($p = 0.06$). There was no statistically significant difference in survival of patients with diffuse type compared to patients with mixed type ($p = 0.39$). In multivariate analysis, neither of these two classifications did not have independent prognostic significance.
Conclusion: Ming classification was significant prognostic parameter in patients with gastric adenocarcinoma, but not independent.

PS-13-104
Analysis of IL-6/leptin induced MAPK pathway with Stat3 phosphorylation and intratumoural iNOS expression in colorectal cancer: The preliminary results
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Objective: The Jak/Stat3 pathway especially with a share of Jak2 subunit contributes in genesis and progress of CRC via MAPK pathway. It is believed that chronic inflammation induces NO production both by cancer cells and inflammatory cells as well. An excess of NO could be responsible for damage of DNA and additional molecular events. Seemingly, IL-6 plays at least dual role in CRC progress therefore studying of Jak2/Stat3 and iNOS is interesting. The purpose of present study was a study of activated Stat3 pathway with apparently independent iNOS contribution in colorectal cancer.
Method: To the retrospective study have been enrolled 156 cases of colorectal cancer. All requested data were tabulated and tumours were reevaluated according to principles of TNM 7ed. An immunohistochemical analysis has been performed with Stat3, iNOS and in a moiety of cases with Jak2.
Results: The data show a massive Stat3 nuclear overexpression and 20 % frequency of iNOS expression. The preliminary analysis of phosphorylated Jak2 unexpectedly unveiled nuclear downstream also that protein but in some cases we noted discrepancy with Stat3. All of that could suggest another the Stat3 trigger involved. The statistical evaluation and its meaning is in progress at this moment.
Conclusion: The preliminary analysis points evident role of Stat3 pathway in CRC but dominance of Jak2 phosphorylation and downstream as triggering factor should be under discuss.

PS-13-106
Microsarellite instability in colorectal cancer is associated with immature phenotype of dendritic cells and higher expression of STAT3 and IL-6
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Objective: Microsatellite instability (MSI) or replication error phenotype in colorectal cancer (CRC) is histologically characterized by high lymphocyte density. Murine colon carcinoma conditioned medium induced activation of STAT3 transcription factor, which was associated with an accumulation of immature myeloid cells and an inhibition of the maturation of dendritic cells (DCs). IL-6 was a potent suppressor of DC activation/maturation through STAT3 phosphorylation.The aim of the study was to analyze mature and immature DCs and their association with STAT3- and IL-6-possitive cells in tumour microenvironment (TME) of CRC with MSI.
Method: Using immunohistochemistry we investigated group of patients with CRC for expression of CD1a, IL-6 and STAT3.
Results: MSI was associated with increased number of CD1a (immature) DCs and with elevated numbers of STAT3- and IL-6-possitive immune cells.
Conclusion: In MSI patients tumour-infiltrating DCs were mainly with immature phenotype and probably their maturation was suppressed by high STAT3 and IL-6 expression in TME.

PS-13-107
Paradoxical expression of claudins in adenocarcinoma and premalignant lesions of the colon and rectum
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Objective: Claudins are members of membrane tight junction proteins. They play critical role in cellular proliferation and neoplastic transformation via their functioning as transmitters of the extracellular stimuli to intracellular signaling pathways.
Method: Samples of 32 colon adenocarcinomas and 86 premalignant lesions (according to WHO classification, 2010) were included in this study. The aim was the immunohistochemical evaluation of claudin-1, claudin-3 and claudin-4 localisation.
Results: Typical membrane localisation of claudin-1, claudin-3 and claudin-4 was detected in 84, 64 and 52 cases respectively. Paradoxical cytoplasmic expression of claudin-1 was found in 33 cases, claudin-3—in 50 cases, claudin-4—in 66 cases; incidence in adenocarcinoma was statistically higher ($p < 0,05$). Nuclear localisation was observed relatively rare. Nuclear expression of claudin-1 was not detected. Nuclear expression of claudin-3 was detected in 2 cases of adenocarcinoma, reaction was diffuse and isolated. Nuclear expression of claudin-4 was detected in 10 cases from different types of premalignant lesions except hyperplastic polyps, reaction was focal and associated with cytoplasmic and membrane reactions.
Conclusion: Nuclear expression of claudin-3 in colon adenocarcinoma and claudin-4 in premalignant lesions were detected for the first time. The nuclear translocation of claudins potentially may play a role in carcinogenesis. The possible mechanisms of this translocation are unknown.

PS-13-108
Comparison of cytoplasmic and nuclear expression of CD133 between colorectal adenoma and adenocarcinoma with clinicopathological assessment in adenocarcinoma
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Objective: Eighty percent of colorectal adenocarcinoma (CRAC) develop step- by- step, known as adenoma-carcinoma sequence. CD133 has been suggested as a potential marker of CSCs. The aim of our study was to compare the CD133 expression between adenoma and CRACs in terms of adenoma-carcinoma sequence, and to investigate the clinicopathological value of CD133 expression in CRACs as a prognostic marker.
Method: 61 adenomas and 166 CRACs arranged as tissue microarray were examined using immunohistochemistry for CD133 expression. The cytoplasmic and nuclear expression of CD133 were scored by semiquantative method and compared between adenomas and CRACs. Correlation of CD133 expression with clinicopathological parameters was also verified in CRACs.
Results: The adenomas showed significantly lower cytoplasmic and nuclear CD133 expression than did the CRACs ($p < 0.001$). The CRACs located in descending colon showed lower cytoplasmic expression of CD133 than did CRACs located in other sites ($p = 0.037$), and the nuclear expressions of CD133 were lower in the CRACs which made recurrence or distant metastasis than the rest without it ($p = 0.032$). The disease-free survival showed a tendency of low cytoplasmic and nuclear expressions

of CD133 were related to disease progression, of which nuclear one was negatively correlated with disease-free survival in log-rank ($p = 0.036$).
Conclusion: CD133 expression in cytoplasm and nucleus seems to be a intermediate step occurring in colorectal carcinogenesis, and nuclear expression in CRACs is a good prognostic marker in terms of recurrence / distant metastasis and disease-free survival, which makes the reasoning possible that CD133 may play a role certain carcinogenesis step mostly, especially early carcinomatous stage, and progressly shows a decreased expression with CRACs progression.

PS-13-111
Expressions of GSTT1, GSTM1 and p53 in human gastric tumour and non-tumour tissues
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Objective: Nutritional, infectious and genetic factors have been shown to play a role in multistage process of gastric carcinogenesis. Also, several lines of evidence have indicated that cigarette smoking is a risk factor for developing gastric cancer and that the carcinogens in tobacco smoke, such as benzo[α]pyrene and drinking water are involved in gastric carcinogenesis. Glutathione S-transferases (GSTs) are involved in the metabolism of many xenobiotics, including an array of environmental carcinogens, chemotherapeutic agents and endogenously derived reactive oxygen species.
Method: In this study we investigated the immunohistochemical staining characteristics of GST Mu-1 (GSTM1), GST Theta-1 (GSTT1), p53 in gastric tumour and surrounding tumour free (normal) gastric tissues from 40 patients. For immunohistochemical studies, tissues were obtained from 40 patients with gastric adenocarcinoma. Tumour and gastric tissues of patients were compared according to their staining intensity. Relationships between p53 and GST expressions in adenocarcinoma tissue were examined by the Mann Whitney-U test, and the clinicopathological data were examined by the Spearman correlation rank test.
Results: GSTM1, GSTT1 and p53 expressions in gastric cancer cells were significantly higher than those in colon normal epithelial cells ($p < 0.05$). No significant relationship was found between the studied isoenzyme expressions and age, gender, smoking status, tumour grade and tumour stage ($p > 0.05$).
Conclusion: In gastric cancer patients the higher expressions of GSTM1, GSTT1, and p53 proteins in tumour than normal gastric tissues could be important in colon cancer progression and development.

PS-13-112
Genotyping-RAS mutations analysis in colorectal cancer
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Objective: Colorectal cancer (CRC) is the third most commonly diagnosed cancer and important leading cause of cancer death among both men and women. The management of this widely prevalent cancer, have indicated that the selection of anti-epidermal growth factor receptor (EGFR) therapy, can improve survival rates for those patients whose tumours do not have RAS mutations (K-RAS and N-RAS oncogenes).
Method: Therefore we analyzed mutations in exons 2, 3 and 4 of K-RAS and N-RAS oncogenes on formalin-fixed, paraffin-embedded tissue from the 51 patients with primary tumour in the colon or rectum or a metastasis. The majority of these tumour samples were from primary tumour rather than from biopsies of metastatic sites.
Results: Approximately half of patients with CRC have RAS wild-type tumours and half have RAS mutant tumours. RAS mutation prevalence was higher in females versus males (58.6 % versus 41,4 %). The most frequent location for RAS mutations in CRC patients was KRAS exon 2 (c.35G>T or c.35G>A) and only one case showed c.182A>G mutation in exon 3 of N-RAS oncogene.
Conclusion: Pathologists have a crucial and responsible role in coordinating RAS testing as mutation analysis is performed on paraffin-embedded tissue selected by the pathologist. The additional analysis of KRAS and NRAS genes as predictive markers can allow more accurate selection of patients who are more likely to benefit from anti-EGFR antibody therapy.

PS-13-114
The influence of radiotherapy on tumour morphometry in rectal carcinoma
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Objective: The authors compared a set of morphometric parameters of two distinct groups of rectal carcinomas, divided by the presence of preoperative irradiation.
Method: The studied material consisted of longitudinal and cross sections of 34 non-irradiated and 25 irradiated rectal tumours, fixed in buffered formalin, included in paraffin, and stained with hematoxylin-eosin. The mean values of tumour diameters (longitudinal and transverse), tumour maximum height related to mucosal surface, maximum tumour invasion, ulceration (when existed) maximum depth and tumour migration under the normal mucosa around the tumour (proximally, distally and laterally) were determined with image analysis software.
Results: The obtained data showed decreasing of tumour diameters and height either it was ulcerated or not and reduction of ulceration depth (when existed) in irradiated tumours. Also, tumour migration under normal mucosa was reduced in irradiated tumours, especially proximally to the tumour. However, the lateral tumour migration and the depth of tumour invasion seemed not to be influenced by the irradiation. The latter could be explained by the taking into account of the deepest tumour cells found even they had degenerative changes caused by the irradiation.
Conclusion: Tumour proliferation is influenced by the preoperative irradiation who determines the reduction of all tumour dimensions and of invasive process.

PS-13-115
Comparison of diagnostic power between traditional mitotic ratio and digital image analysis of Ki-67, p21, p27 and cyclin D1 in GIST
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Objective: Advancement of technology provides many additional tools to study of their usefulness also in medicine field. Limitation of the human eye and awareness of randomness in mitotic figure counting dispose to looking for objective feedback such as digital image analysis. The purpose of present study is facing to traditional way of prediction based on mitotic ratio in comparison with digital image analysis of cell cycle dependent proteins
Method: 56 cases of GIST were reanalyzed at one traditional histopathological way with categorisation to two groups 0-5 and above 5 mitotic figures within 50hpf. Parallel, there have been performed immunohistochemical assays with Ki-67, p21, p27 and cyclin D1. Whole slides were scanned using slide scanner Hamammatsu NanoZoomer S60 with consequent digital image analysis using Visiopharm software. We performed double analysis within hot-spot and not hot-spot foci
Results: Ki-67 hot spot positive ratio (HSPR) with threshold at 0,27 split up low and high risk ESMO groups (ESMO ≤ 3 i ESMO > 3)

($p < 0.00001$). We noted hard evidences of Ki-67 ratio usefulness to predict the clinical outcome. The achieved data present Ki-67 HSPR correlation with average mitotic score: ≤ 5 vs. >5 ($p < 0.0001$), tumour size ≤ 5 cm vs. > 5 cm ($p = 0.036$), location "gastric" vs. "non-gastric" ($p = 0.044$), and also previously described GLUT-1 ($p = 0.0002$) and CD63 ($p = 0.0003$)
Conclusion: Ki-67 ratio labelling is a useful tool in splitting up of low and high grade GIST

PS-13-117
The impact of IMP3 and p53 expression in development of gastric cancer
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Objective: The p53 protein is a molecule with numerous functions. However, mutation of p53 and accumulation of mutated p53 protein, which have no normal function, are common in human cancers. In addiction Insulin-like Growth Factor-II mRNA-Binding Protein 3 (IMP3) may be implicated in the pathogenesis of the tumours, since it is expressed in neoplastic tissue. The aim of this study is to investigate p53 value and it relationship with IMP3 expression, clinicopathological parameters and survival in patients with gastric cancer.
Method: In 44 patients who had undergone gastrectomy for gastric cancer, the expression of p53 and IMP3 in tumour tissues were examined immunohistochemically. The clinicopathological parameters and survival were analyzed retrospectively.
Results: We found p53 expression in all of gastric cancer specimens. Also, 23.6 % of specimens were IMP3 expression positive. Our data demonstrate a relationship between survival and p53 expression. The patients with p53 expression had worse prognosis after surgical therapy compared to those without. The median survival of p53-positive patients was 4.8 months whereas the median survival of p53-negative patients was 9.1 months ($p = 0.027$; log-rank test). Also, 37.8 % from patients with p53-positive status is in T1-T2 stage vs. 88.9 % in T3-T4 ($\chi 2 = 7.88$, $p = 0.005$). The data was similar for IMP3 expression, but without significance.
Conclusion: In conclusion our results suggest that expression of p53 and IMP3 could be useful as a marker of poor prognosis and had prognostic value for gastric cancer patients.

PS-13-118
Immunohistochemical evaluation of p53 in premalignant lesions of the colon and rectum
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Objective: The TP53 gene is a classic tumour-suppressor gene. The p53 protein from abnormal TP53 gene has a longer half-life, accumulates inside cells and is a marker of malignant transformation.
Method: We assessed immunohistochemical expression of p53 in 28 hyperplastic polyps (HPs), 30 sessile serrated adenomas (SSAs), 15 traditional serrated adenomas (TSAs), 30 tubular adenomas (TAs) and 28 tubulovillous adenomas (TVAs).
Results: The aberrant expression of p53 (>5 % cells) was detected in 26.1 % HPs, 30.0 % SSAs, 33.3 % TAs, 60.7 % TVAs and 73.3 % TSAs. In all HPs and SSAs p53 positive cells were located in lower part of the crypts; in TAs, TVAs and TSAs - in superficial half or throughout the crypts. Pattern of distribution was similar between HPs and SSAs, TSAs and TVAs, TVAs and TAs ($p < 0.05$). Medium amount of p53 positive cells was 6.6 % in HPs, 6.0 % in SSAs, 10.5 % in TAs, 26.5 % in TVAs and 25.4 % in TSAs.
Conclusion: Summarized patterns of p53 expression are similar between TSAs and TVAs, HPs and SSAs ($p < 0.05$). According to p53 expression levels TSAs and TVAs show the highest malignant potential, HPs and SSAs—the lowest, TAs show intermediate features. The reported study was funded by RFBR according to the research project №16-34-00179 mol_a.

PS-13-119
High grade non-Hodgkin B cell lymphoma in the sinuses of regional lymph nodes in a patient with colorectal cancer
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Objective: We report a case of a 73-year-old woman with a colon adenocarcinoma, with no regional lymph nodes metastasis, in which sinuses we found a non-Hodgkin high grade B cell lymphoma. As we know no such case has been described. In literature eight cases of colorectal adenocarcinomas and lymphomas as collision tumours, three cases of lymphoma following colorectal cancer and two cases of synchronous intravascular lymphoma with meningioma and breast cancer are reported.
Method: We received a right hemicolectomy with a tumour measuring 11,5x5cm. We found twenty three lymph nodes in mesenteric and thirty eight in pericolic fat.
Results: Histological examination revealed a colon adenocarcinoma with extension into pericolic fat without nodal metastasis. The majority of the lymph nodes had large atypical lymphoid cells in their sinuses, staining diffusely positive for CD79a, CD20, PanB, focally for CD30 and PAX5 and negative for CD3, CD5, Bcl2, Bcl6, ALK and EBV. Ki-67(MIB1) was estimated 75 %. A diagnosis of diffuse large B-cell lymphoma (DLBCL) was made. We discussed the possibility of an intravascular large B-cell lymphoma but bone marrow biopsy and CT scan revealed no other lymphoma localisation.
Conclusion: Pathologists must be aware of synchronous malignancies, particularly lymphomas, when examining and staging lymph nodes for cancinomas.

PS-13-120
Multifocal metastasis of amelanotic melanoma to the small intestine from an unknown primary
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Objective: The aim of this study is to point out an unusual presentation of a metastatic malignant melanoma throughout the jejunal and ileal wall.
Method: We present the case of a 62 year old patient, admitted to the gastroenterology department with abdominal distension and pain, hemodinamically anemic. A CT scan revealed five jejunal and ileal nodular haemorrhagic tumours, treated surgically, with an uneventful recovery.
Results: The gross examination showed 5 nodular ulcerated tumours between 0.5 and 3 cm throughout the jejunal and ileal wall. The microscopic examination showed a malignant proliferation with a diffuse, solid and trabecular architecture, with high celular and nuclear pleomorphism and abundant tumour necrosis, negative for AE1/AE3, LCA, CG-A, Syn and NSE, with a high mitotic rate Ki67 of 70 %. Further tests revealed a melanocytic immunophenotype with diffuse positivity for S100, HMB45 and MART1, thus establishing the diagnosis of multifocal metastatic melanoma.
Conclusion: Malignant melanoma is a major health concern in developed countries, due to recreational UV Radiation exposure. Metastatic melanoma should be included in the differential diagnosis even though the patient has no history of skin disease.

PS-13-121

Digestive and mesenteric gastro-intestinal stromal tumours: A monocentric retrospective study

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Objective: To describe epidemiologic and clinicopathological features of gastro-intestinal stromal tumours (GISTs).
Method: We performed a retrospective study of 15 GISTs diagnosed at the department of Pathology. Tumour risk of recurrence was determined according to Miettinen and Lasota classifications.
Results: Our study included 8 female and 6 male with a median age of 61 years. The tumour was located in the stomach (n = 6), the jejunum-ileum (n = 3), the duodenum (n = 2), the mesentery (n = 2) and the rectum (n = 2). The median tumour size was 9.8 cm. Histologically, the spindle cell type was the most common (86 %), followed by the epithelioid type (7 %) and the mixed one (7 %). GISTs displayed a strong and diffuse positivity for CD117 (53 %), CD34 (73 %) and DOG1 (46 %). Forty per cent of GISTs were at a high-risk of recurrence, 13 % at a moderate risk, 20 % at a low risk and 20 % at a very low risk.
Conclusion: GISTs must be mainly distinguished from leiomyoma and schwannoma since prognosis is different. Diagnosis is based on histology but requires immunohistochemistry and in some cases a molecular study. Estimation of the risk of recurrence is compulsory, as there is a therapeutic impact by using the tyrosine kinase inhibitors.

PS-13-122

Synchronous goblet cell carcinoid and colonic adenocarcinoma: A rare coexistence

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Objective: Goblet cell carcinoid is known to be a rare and combined form of carcinoid tumour. It is nearly exclusive to appendix and has both features of adenocarcinoma and carcinoid tumour. This variable morphologic features lead to an intermediate outcome. Here we present a case of goblet cell adenocarcinoid in appendix and a synchronous colonic adenocarcinoma.
Method: Seventy-six years old male patient has undergone right hemicolectomy due to ascending colon tumour. In gross examination tumour was identified as 4x4 cm, tan to grey polypoid mass infiltrating the pericolic fat. No other pathologic finding was recorded in adjacent structures.
Results: In microscopy the patient had a high grade colonic adenocarcinoma with subserosal invasion and besides usual adenocarcinoma morphology, tumour had 4 % mucinous component. Additionally in appendix, there was a tumour of 3 cm composed of adenocarcinoma like tumour cells and also scattered atypical goblet cells and single cells occasionally forming clusters. Carcinoma component was approximately 50 %. Mesoappendix invasion and lymphovascular invasion were identified as well as a mitotic rate of 3/10HPF. Immunhistochemically tumour cells were stained with Chromogranin A and synaptophysin and CK20 positivity was seen in only some tumour cells. The case was reported as colonic adenocarcinoma and pT4 goblet cell carcinoid tumour.
Conclusion: Goblet cell carcinoid is a rare neuroendocrine tumour type nearly exclusive to appendix. Since its unique structure involves both features of adenocarcinoma and NET, it has a prognosis between the two entities. There is no generally accepted guideline for management of this tumour. Treatment options varies between simple appendectomy or right hemicolectomy.

PS-13-123

Perineurial-like stromal proliferations in sessile serrated adenomas of the colon

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Objective: The presence of perineurial-like stromal proliferations in serrated polyps of the colon is a rare phenomenon, suggesting epithelial-stromal interactions. The aim of our study was to evaluate this kind of proliferation in sessile serrated adenomas of the colon.
Method: We evaluated the pathologic characteristics of sessile serrated adenomas diagnosed in our department during the last 4 years.
Results: Four out of 85 patients, 2 males and 2 females, ranging in age from 43 to 75, with one or more polyps located in ascending and transverse colon, exhibited perineurial-like stromal proliferations. Histologically, these were defined as bland, uniform, spindle cell proliferation within the lamina propria or submucosa, showing a striking pericryptal growth pattern, which were immunohistochemically positive for EMA and negative for S-100 protein.
Conclusion: The striking pericryptal growth pattern of perineurial-like proliferations in some serrated polyps of the colon is indicative of an intimate interaction between these stromal cells and serrated colonic epithelium. However, the origin of this unique stromal proliferation is still unclear and the association with serrated polyps, including sessile serrated adenomas, has not been fully described. One possible explanation is an epithelial-stromal interaction, possibly related to some factors elaborated by the serrated epithelium.

PS-13-124

Tuberculous versus Crohn's anal fistula: Diagnostic difficulties in endemic area

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Objective: Crohn's disease and intestinal tuberculosis are frequently misdiagnosed due to their high similarity. The aim of the study was to illustrate diagnosis difficulties of tuberculous versus Crohn's anal fistula.
Method: We describe four cases of isolated anal fistula without past medical history of tuberculosis or Crohn's disease. Clinical, laboratory, endoscopic, radiographic and histologic features and therapeutic issue were determined.
Results: Our series consisted of three men and one woman aged between 25 and 52 years. The most common symptoms were a non healing simple or complex perianal fistula. Colonoscopy had been performed in all patients and they were visually normal. The signs of tuberculosis impregnation were present in 2 patients. On microscopic examination, only one case presented a caseating granulomas. TST/IGRA were positive in all cases. As results, half of cases was associated with clinical deterioration. One patient was healed and one not.
Conclusion: Differenciation between perianal tuberculosis and crohn's disease is a challenge, particulary in endemic country. Clinical pictures of both are similar and any test can distinguish between them with sufficient sensibility and sensitivity.

PS-13-127

Circadian rhythm proteins dysregulation in colorectal carcinoma

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Objective: Basic principles of circadian rhythms is a periodical activation of genes, with a feedback autoregulation mechanism of their expression.

Disruption of the circadian rhythm is becoming a hallmark of the modern life style. CLOCK genes control expression of clock-targeted genes, deregulation of which may contribute to tumourigenesis. Some studies pointed at correlation between expression of clock genes and biological behavior of neoplasms. The present study evaluated changes in expression of some CLOCK genes protein products in colorectal carcinoma.
Method: Colorectal carcinoma surgical specimens (No) were immunohistochemically evaluated for protein expression of Per1, Per2, Cry2, Timeless and Clock. Expression of the immunoreactivity with specific monoclonal antibodies was evaluated semiquantitatively with calculating a percentage-intensity quick score.
Results: Neoplastic colorectal carcinoma and nonneoplastic tissue specimens from 76 patients showed tumour tissue significant decrease of Per1 and Timeless expression, increased Per2 and no change in expression of Cry2 and Clock.
Conclusion: The presented data support the view that changes in circadian rhythm proteins expression are involved in cancerogenesis. Detection of these proteins might help to better understanding of the disease and serve as potential therapeutic targets. Supported by APVV-14-0318

PS-13-129
Rule of concentration of stromal mast cells in different type of intestinal adenoma
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Objective: The aim of this study was to determine the density of stromal mast cells in different types of intestinal adenomatous polyp and its protective role in tumourogenesis.
Method: Eighty paraffin blocks with a diagnosis of adenoma were stained with toluidine blue and Mast cell density was counted in approximately 1 mm2 at the edge of lesions. Patients were classified in three groups (mast cell density <30, 30–60 and > 60).
Results: In mild dysplasia, 62.5 % were under 30, and 37.5 % were between 30 and 60 and none of the cases with mild dysplasia; in moderate dysplasia, 12.9 %, under 30, 68.8 % were between 30 and 60 and 18.6 % greater than 60; In severe dysplasia, all cases had mast cell densities greater than 60 ($P < 0.0001$). In all three types of adenomas, the largest number of samples had mast cells density between 30 and 60 that included 61.9 % of samples in tubular type, 69 % in tubulo-villous type and 55.6 % of samples in the villous type and was not statistically significant ($P = 0.21$).
Conclusion: The density of mast cells increases with increasing the histological dysplasia degree . These findings can be very useful in choosing the safe margin for tumour resection.

PS-13-130
Elastic fibers and venous invasion in colorectal cancer
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Objective: Venous invasion (VI) is a well-established independent predictor of hematogenous spread of colorectal cancer (CRC). The aim of our study was to evaluate the changes of stromal elastic fibers in CRC and to establish correlations with venous invasion.
Method: Analysis of clinical data from 44 patients diagnosed with colorectal cancer followed by stratification into groups based on TNM classification. Light microscopy of tumour tissue slides stained with H&E, histochemical analysis of slides stained with Russell-Movat pentachrome.
Results: Distribution of patients according to the TNM classification is following: 1st group (T1-4N0M0) 18/40.9 %, 2nd group (T1-4 N1-2 M0) 16/36.4 % and 3rd group (T1-4 N0-2 M1) 10/22.7 %. Venous invasion was seen in 4 cases (22.2 %) of 1st group, 12 cases (75 %) of 2nd and 8 cases (80 %) of 3rd group. Increase of thickness of elastic fibers around vessels was seen in 11 cases (61.1 %) of the 1st group, in 13 cases (81.25 %) of the 2nd and 9 cases (90 %) of the 3rd group. Gamma's correlation analysis revealed the associations between an increasing of thickness of elastic fibers and venous invasion ($r = 0.42$, $p < 0.05$).
Conclusion: Evaluation of the thickness of elastic fibers around vessels wall is helpful for routine histopathology practice and could be used to predict the behavior of CRC.

PS-13-132
Digestive neuroendocrine tumours: A retrospective study of 33 cases
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Objective: Our objective was to study the pathological features and the immunohistochemical profile of digestive NETs and to classify them according to WHO 2010.
Method: This was a retrospective study of 33 cases of digestive NETs in the department of pathology of the Mongi Slim hospital over a period of 14 years (2003–2016). We analyzed pathological, immunohistochemical and outcome.
Results: The average age of our patients was 35,84 years with a sex ratio of 0,5. The NETs in our series were appendicular (19 cases), pancreatic (13 cases) and gastric (1 cases). They were classified according to WHO 2010 as: grade 1 NETs in 30 cases (91 %), grade 2 NETs in one case (3 %) and grade 3 NETs in two cases (6 %). Treatment was surgical in 100 % of cases. Only one patient died in the immediate postoperative period. The follow-up period varied from 1 to 10 months with an average of 3 months. No tumour recurrence or distant metastasis had occurred.
Conclusion: Digestive NET is a heterogeneous group of tumours with a very broad prognostic spectrum. The diagnosis of certainty and grading of digestive NET is based on histological examination coupled with an immunohistochemical study.

PS-13-133
Collision malignant melanoma and adenocarcinoma of the anorectum - a case report
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Objective: A collision tumour consists of two coexisting but independent tumours. It is extremely rare in the gastrointestinal tract. Most are carcinoid tumour admixed with adenocarcinoma, or adenocarcinoma combined with lymphoma. Here, we report a case of collision malignant melanoma and adenocarcinoma of the anorectal junction.
Method: A 74-year old female patient presented with a change in bowel habit and fresh per-rectal bleeding. The initial diagnostic biopsy showed a poorly differentiated tumour with malignant melanoma component present at the anorectal junction. She underwent abdominoperineal excision of the rectum and made a full postoperative recovery.
Results: The histology demonstrated a biphasic tumour with the morphology of both malignant melanoma and adenocarcinoma, which was confirmed by immunohistochemical analysis. A local lymph node was also involved. Unfortunately, follow-up imaging 5 months later showed metastatic deposits in both adrenal glands. She was referred to oncology for further treatment.
Conclusion: A literature search confirms the rarity of these tumours. To the authors' knowledge, there is only one other case reported to date. Based on the available data, the consensus is that the prognosis should be defined by the most aggressively malignant component; therefore, the treatment strategy was focused on treating the malignant melanoma.

PS-13-134

Amyloidosis presenting in the gastrointestinal tract of a patient with coexistent duodenal lambliasis

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Objective: To report a case of a 66 years old man, with lambliasis in the duodenum and amyloid deposits as first clinical presentation of amyloidosis.
Method: The patient presented with weight loss and epigastric discomfort. During gastric and colonic endoscopic examination the only finding was antrum gastritis. Microscopically, in the gastric mucosa mild chronic gastritis with mild glandular atrophy was observed. There was abundance of the parasite Giardia lamblia in the duodenum accompanied with moderate inflammatory infiltration. At the same time, we observed expansion of the villi in the duodenum and eosinophilic substance in the lamina propria in the duodenum and in the antrum. Congo Red stain confirmed this eosinophilic substance as amyloid deposition.
Results: The patients' bone marrow was examined and no plasma cell dyscrasia or amyloid deposits were found. Systemic amyloidosis was excluded from further examination.
Conclusion: Localized amyloidosis of the gastrointestinal tract is extremely rare. In our case we considered if Giardia lamblia could, in any case, produce proteoglycans to induce secondary amyloidosis but we found no previous data to support such hypothesis.

PS-13-136

A case report of goblet cell carcinoid accompanied by ulcerative colitis

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Objective: The goblet cell carcinoid (GCC) is a rare tumour of the gastrointestinal tract. GCC almost exclusively occurs in the appendix but may occasionally be found in other parts of the gastrointestinal tract.
Method: We report a case of GCC with ulcerative colitis. A 68 years old man, has had ulcerative colitis since 2013, was admitted to our gastroenterology for control colonoscopy. In rectum, there was an ulcer in size of 25–30 mm.
Results: Histologic evaluation confirmed ulcerative colitis. In addition, there was a tumour composed of small acini and individual cells with intracytoplasmic mucin. The tumour was positive with the CDX2 and neuroendocrine markers chromogranin, synaptophysin and CD56. The diagnosis was GCC of the rectum with co-existing ulcerative colitis.
Conclusion: GCC is a clinicopathologically distinctive tumour that typically arises in appendix. Rectal location and association with ulcerative colitis are very rare. Its differentiation from signet ring cell carcinoma has significance regarding outcome and patient management.

PS-13-137

Granular cell tumour of the cystic duct of the gallbladder: Case report

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Objective: Granular cell tumour (GCT) is a benign tumour of neuroectodermal origin. Although it is the most common benign non-epithelial tumour of the gallbladder and billiary tract with young female predominance, it is relatively rare with only 81 reported cases in the literature.
Method: We report a case of a GCT of the cystic duct of the gallbladder. We received a cholecystectomy surgical specimen from a 28 year old female patient. The major macroscopic finding was the asymmetrical thickening of the wall of the cystic duct.
Results: The microscopic examination revealed nests of oval or polygonal neoplastic cells with abundant eosinophilic periodic acid-Schiff (PAS)-positive granular cytoplasm, indistinct cell borders and small nuclei without atypia. The neoplastic cells infiltrated the muscular layer of the cystic duct wall. Immunohistochemically the cells were diffusely positive for S-100 protein, NSE, CD68/KP1, Inhibin-a, Nestin, PGP9.5, SOX-10 and negative for micropthalmia transcription factor, TFE3, SF1, Olig2, NeuN, Calretinin. Based on the morphological and immunohistochemical findings the diagnosis of granular cell tumour was established.
Conclusion: Granular cell tumour is hypothesized to originate from a Schwann-like mesenchymal cell and it rarely affects the biliary tract but can lead to obstruction and secondary biliary cirrhosis if left untreated.

PS-13-138

Adenocarcinoma of the pancreas metastatic to the breast: A case report

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Objective: Metastasis to the breast from extra mammary carcinoma is uncommon, peculiarly from pancreatic malignant disease. Clinical and radiologic findings are no specific. Often metastases to the breast show histological features, suggestive of the original cancer but that is not always true and processing to immunohistochemistry seems to be a helpful means of diagnosis.
Method: We report the case of a 63-year-old patient recently diagnosed with a metastatic pancreatic cancer.
Results: On clinical examination we found a right mammary, subcutaneous nodule. It was mobile, firm and measuring 1.5 cm long axis, at the under outer quadrant. A mammogram revealed a deep nodule, dense and relatively well limited measuring 1x1cm. It was classified ACR4. The patient had a lumpectomy. In the frozen section, an infiltrating carcinoma was found. At the final examination, a cancerous tumour proliferation of glandular and trabecular architecture with tumour necrotic foci was noted. Immunohistochemical study showed that the tumour cells are CK7 +, CK19+, CK20-, CEA focally positive, HR-, HER2 score 1+. We concluded at a metastasis to the breast of a pancreatic adenocarcinoma.
Conclusion: Adenocarcinoma of the pancreas metastatic to the breast is one of the rarest primary cancers that disseminate to the breast. It is an aggressive malignancy with poor prognosis, regrettably diagnosed in final metastatic stages. Establishing an accurate diagnosis is important in order to preclude unnecessary mastectomy and provide suitable systemic treatment.

PS-13-139

A rare lesion of stomach gastritis cystica polyposa/profunda, report of two cases

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Objective: Gastritis cystica polyposa/profunda is a rare lesion .It can be presented with a wide clinical spectrum Although the causes are not clear, the most common factors are bile reflux and previous stomach operations.
Method: Here, we present two cases diagnosed in our clinic:
Results: Case 1: A 72 year-old female patient have a diagnosis of hyperplastic polyp in another center applied to clinic. Endoscopy had been performed in our clinic showed a 3 cm granulated polyp prolapsed from antrum to bulbus. Microscopic evaluation revealed cystic, well-structured glands in muscularis mucosa. Case 2: A 45 year-old female patient presented to clinic due to hiccup for 3 months. Ultrasonographic examination showed a lesion interpreted as submucosal mass. The patient was operated due to preoperative diagnosis of GIST . Macroscopic examination showed a mass lesion under the mucosa. Microscopic examination revealed nodular, cystic dilated, well-structured glands, placed in

muscularis propria. Both glands were mucinous, covered with a rim of lamina propria and did not contain structural/cellular atypia. Both cases were diagnosed as gastritis cystica polyposa/profunda.
Conclusion: we present two cases of gastritis cystica polyposa/profunda with different preoperative findings, and want to remind in the differantial diagnosis of the mass/polypoid lesions of the gastric wall.

PS-13-141
Opportunistic viral infections of upper gastrointestinal truck: Three case reports
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Objective: Opportunistic infections caused by cytomegalovirus(CMV) and herpes simplex virus(HSV) are commonly seen in immunocompromized and high risk patients and are responsible for severe clinical symptoms, such as ulceration, hemorrhage and perforation.
Method: We present the case of a 30-years-old-man, who received high doses of corticosteroids for idiopathic thrombopenic purpura. He complained for gastric pain and during upper GI endoscopy a gastric ulcer and acute gastritis were found. Biopsies showed the characteristic eosinophilic intranuclear and granular-purple cytoplasmic inclusions in epithelial and endothelial cells, findings compatible with CMV gastritis
Results: The other two patients, a 86-years-old-man and 82-years-old-woman, complained for dysfagia and retrosternal pain. They both had no-clinical evidence of immunosuppression, but they were often hospitalised. Esophagoscopy revealed white plaques, linear erosions and ulcer. Histological examination showed acute inflammation, ulcers and typical epithelial intranuclear inclusions and ground glass multinucleated giant cells, all suggestive of herpetic oesophagitis. After PCR certification, antiviral therapy was given.
Conclusion: The clinical history and the unusual endoscopic findings may guide pathologist to careful examination of the tissue sample and recognition of typical cells suggestive of specific viral infections, diagnosis crucial for patient s life. Immunohistochemistry could be used in cases that morphology is not typical. Cultures and PCR could also be helpful.

Tuesday, 5 September 2017, 09:30–10:30, Hall 3
PS-14 IT in Pathology

PS-14-001
A comparison of labeling index Ki67 determined by image analysis software and visual assessment in breast cancer
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Objective: The labeling index (LI) Ki67 is critical part of the pathology practice for the diagnosis and prognosis in breast cancer. In this study we compared the consistency between visual assessment (VA) and digital image analysis (DIA) LI Ki67 in breast cancer in the laboratory of tumour morphology of N.N. Petrov Cancer Research Institute.
Method: Ki67-immunostained slides of 106 cases of breast cancer G-2-3, mean age 64,2 randomly selected from July to September 2016 in the pathology department. In these study two different score methods were used: DIA and VA by two experts and one resident of 1 year independently of each other.
Results: The level of agreement between the DIA and VA was not significantly different ($p > 0.005$), the intra-class correlation coefficient (ICC) between the DIA and VA method was 0.69 CI 95 %, [0.23; 0.87] – DIA-VA expert 1, 0.72, CI 95 %, [0.33; 0.89] – DIA-VA expert 2, 0, 70, CI 95 %, [0.30; 0.88] – DIA-VA resident.
Conclusion: The values of LI Ki67 obtained by the DIA showed a strong correlation with the expert values of the LI Ki67.

PS-14-002
Discrepancy of labeling index Ki67 in ER positive HER2 negative breast cancer determined by image analysis software and visual assessment
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Objective: We compared two different subgroups (luminal A and luminal B) based on IHC surrogate classification by digital image analysis (DIA) and visual assessment (VA) of labeling index (LI) Ki67. LI Ki67 is widely used for clinical decision making in luminal A and luminal B (St. Gallen Consensus 2015). Cut-off point widely used in this approach is 14 %.
Method: We selected 45 cases HER2- ER+ of breast cancer G-2-3, mean age 58,3 in the pathology department. In this study two different score methods were used: DIA and VA to compare consistency by intraclass correlation coefficient (ICC) in luminal A and luminal B subgroups.
Results: Among 45 breast cancer cases there was luminal A 46 % and luminal B 54 % of cases according to DIA but using VA LI Ki67 luminal A was 22 % and luminal B was 78 % respectively. Reproducibility was poor (ICC = 0.157; 95 % CI = [−0.027; 0.541]) in luminal A and luminal B was fair (ICC = 0.46; 95 % CI = [0.082; 0.722]).
Conclusion: Using cut-off point 14 % LI Ki67 in DIA luminal A showed two times often than in VA. LI Ki67 values distribution showed better consistency between DIA and VA in luminal B but poor in luminal A.

PS-14-003
Medical simulation in gross examination: University experience
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Objective: The importance given in recent years to the acquisition of practical skills in medical school is mainly due to the Bologna Process and to the Objective-Structured-Clinical-Examination (OSCE). This new framework implies self-evaluation and a renewal of the teaching methodologies. For this purpose, a practical simulation for the gross examination (GE) was carried out.
Method: Silicone simulators of different shapes, sizes and color combinations were used. The students conducted the GE study in different clinical contexts in a guided approach, including: clinical correlation, sample description, including weight and measurement, use of colored dyes to evaluate surgical margins, sectioning and its inclusion in cassettes. Finally, for the final diagnosis and understanding of macro-microscopic correlation, digitized slides were used. The simulation was developed with third-year medical students from the University of Murcia (2016–17), who were given a Likert scale questionnaire for assessment.
Results: A total of 42 students participated in the simulation. The results of the questionnaire showed an average score of 4.26 on a scale of 5 in the following items: understanding tumour surgery and GE management, assessing surgical margins, microscopic visualization and diagnosis, and prognostic significance.
Conclusion: - Gross examination simulation can serve as a good learning system, in support of traditional methods. - The implementation of these interactive teaching methodologies is well accepted by students. - The experience presented in this study is adapted to the new requirements in medical training, with the acquisition of clinical skills and competencies, while at the same time transmitting a more realistic idea of the work carried out by pathologists.

PS-14-004

Our results creating pathological reports with the GlobalspeechTM speech recognising software

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Objective: The author summarises his experiences with the GLOBALSPEECHTM speech recognising software in creating 14.040 pathological reports.
Method: The software recognises different languages but currently we used to recognise Hungarian and Latin medical phrases. This study includes 1.160 autopsy reports (AR), 1.620 body cavity fluid cytology reports (BCFCR), 2.740 fine needle aspiration cytology reports (ACR) and 8.520 histology reports (HISTR).
Results: The average speech recognition rate of the total dictated 1.185.374 words is 99.38 % (AR: 99.45 %, BCFCR: 99.20 %, ACR: 99.46 %, HISTR: 99.08 %). Currently, based on the last 4020 reports the average recognition rate is 99.69 % (AR: 99.72 %, BCFCR: 99.89 %, ACR: 99.70 %, HISTR: 99.70 %). Our latest results show that there were 0–2 mistakes/page what is regarded to be an acceptable quality of the reports (it is for AR: 90 %, BCFCR: 99.77 %, ACR: 98.35 % and HISTR: 99.38 %).
Conclusion: Our result seems to be better than the 90–95 % speech recognising rate published in the literature. It means that the speech recognising ability of the software is the same as the one of the living speech. Therefore the GLOBALSPEECHTMspeech recognising software is very suitable tool for creating pathological reports.

PS-14-005

Development of a real-time semi-automated anatomic pathology dashboard to facilitate better case tracking and follow up: Another step towards high reliability

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Objective: To describe the development of real-time dashboard to track pending (unsigned) and potentially delayed cases in anatomic pathology.
Method: Several management reports ($n = 8$) within our lab information system (LIS - Cerner CoPath Plus) were set to run daily and automatically save on a network drive. A Visual Basic macro was developed that automatically runs and imports the latest saved LIS report data into a Microsoft Excel file. The Excel file then concatenates the data into a single table for each anatomic pathology section by utilizing formulas that search each report for the accession numbers of unsigned cases. Using predetermined turnaround time goals, cases exceeding a particular age are flagged as delayed.
Results: The dashboard displays a summary worksheet, and more detailed worksheets for each anatomic pathology section. The latter display the accession #, accession date, presence/absence of preliminary report, responsible resident/pathologist, memos and status of any pending special stains, IHC and other procedures within the LIS, among other items. A built in email generator is used to notify team members associated with delayed cases and help prompt action when indicated.
Conclusion: The anatomic pathology dashboard provides a real-time status of pending/delayed cases in the lab and can potentially help address developing issues much earlier. This proactive approach can be used to reduce potential adverse events even before they happen, an important High Reliability practice that further improves quality and patient safety.

PS-14-007

Next generation quality: Using big data and funnel plots to compare pathologist diagnostic rates and identify outliers in 22,176 stomach biopsy specimen parts

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Objective: To assess interobserver variability in stomach biopsies using funnel plots and big data.
Method: A custom computer program was used to extract information from 6 years of free text in-house surgical pathology reports at a large academic hospital. Using string matching, fuzzy string matching (google-diff-match-patch) and hierarchical pruning, the diagnoses were categorized by the signing pathologist. Funnel plots were created using GNU/Octave and the range expected due to sampling (REDS) calculated using the median diagnostic rate (DR).
Results: 22,760 stomach biopsy specimen parts were extracted from 110,970 pathology reports, >99 % of parts were categorized, and accuracy (in 200 pathologists/authors audited parts) was ~98 %. Sixteen pathologists interpreted >200 and together read 22,176 parts. Funnel plots with REDS, using a 95 % and 99.8 % confidence interval (CI), varied by diagnosis; pathologists outside the 99.8 % CI ($P < 0.001$) were few for Helicobacter gastritis (1) and intestinal metaplasia (4), but numerous for reactive gastropathy (12) and normal stomach (13).
Conclusion: Funnel plots are easily interpreted and allow identification of pathologists with diagnostic rates outside the REDS for the number of specimens interpreted. Observational data compliments traditional interobserver variability studies and random audits, and could be utilized in a comprehensive data driven quality management/improvement program.

PS-14-008

CD73 expression in metastatic melanoma

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Objective: CD73 is an ectoenzyme that generates adenosine, an immunosuppressive nucleoside. Recently, CD73 emerged as a potential immunotherapy target. This study characterizes CD73 expression in metastatic melanoma.
Method: Metastatic melanoma biopsies from 114 patients were evaluated by immunohistochemistry (anti-CD73, clone D7F9A) for CD73 expression in tumour cells (TC) (staining extent (1–100 %) and intensity (0–3)) and tumour infiltrating mononuclear cells (TIMC).
Results: Patients comprised 55 men and 59 women (median age: 67.2). Examined metastatic sites included lymph nodes (40 %), skin and subcutaneous tissue (21 %) and various viscera and CNS (39 %). Overall, considering a 1 % cut-off, 62/114 (54 %) samples were CD73-positive (membranous with/without cytoplasmic pattern in most cases) with 20/114 samples (18 %) having >50 % CD73-positive TC. Staining intensity was frequently heterogeneous and tended to correlate to staining extent. CD73 expression did not correlate with gender, age, clinical presentation of primary tumour or location of metastasis. CD73 expression in TC (both extent and intensity) correlated to decreased survival from biopsy ($p < 0.001$). Of the samples containing TIMC (106/114), 35 % presented some staining, the majority in ≤5 % of TIMC.
Conclusion: CD73 is frequently present in the metastatic melanoma milieu and our findings suggest that CD73 expression might be associated with reduced survival.

PS-14-009

Teaching with technology: 3D software in the pathology classroom

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Objective: In 2016, staff of pathology department collaborated with a software company to develop a 3D interactive application for seminars to support undergraduate medical students in studying pathology. The program was structured around 10 modules. At the end of each module the program assessed students based on the modeling of gross changes during the pathological process (stage I) and their understanding of microscopic changes (stage II).
Method: We asked 67 students and 6 instructors from two different universities to participate in multiple pilots of the program (involving two surveys and one focus group conducted in 2016 and 2017). The participants were assessed by the 3D software and after this assessment students were asked to fill in the questionnaire to evaluate the program (and its components) and to express their opinion about the potential applications of the program.
Results: All the respondents mentioned that visualization of the pathological process in the organ contributes to better understanding of the subject. Moreover, many of them suggested that the software could be used as a tool illustrating the processes described in the textbook. Both instructors and students mentioned that the program could represent an alternative to the written or oral classroom test, and a useful tool that allows to prepare for the pathology seminar. During the focus groups, participants also stressed that programme helps with remembering of the stages of the pathological process and changes that appear in the organ.
Conclusion: The integration of the 3D software in the classroom helped to find creative and constructive ways to enhance the learning process for students making a challenging medical subject more approachable.

PS-14-011
Pathology in social media: Recruitment campaign experience
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Objective: Pathologists' role continues to be unknown, not only to the general public, but also to our physician colleagues. Nowadays, the widespread use of Social-Media-Networks (SMN) allows us to present and spread our occupation to society and to the patient, our ultimate goal. A creation of a group dedicated to the promotion of pathology was proposed.
Method: The Spanish Society of Pathology (SEAP-IAP) sent a communication to all its members via email, including an application form offering joining a working-group through Twitter. The campaign was titled #IWantYouForSEAP, and animage of the Nobel-Prize-winning Spanish histopathologist, Dr. Santiago Ramón-y-Cajal, was used together with the slogan, "I Want you" by Montgomery-Flagg. The recruitment period lasted 1 month (August 2016).
Results: A total of 31 applications were received (17-women-/14-men, average age 38.6 years), including 27-pathologists (6-residents), 2-histotechnicians, 1-biologist, 1-administrative personnel. There were participants from 22 cities and 25 different institutions.
Conclusion: - It is possible to promote and motivate teamwork within our discipline through the use of SMN, having a quick turnaround-time. - Although this is an initial inquiry, there are great possibilities and high expectations on behalf of the participants. - Proper use of SMN could help to close the gap between pathologists and society.

PS-14-012
Microscopic image stitching for cytopatological analysis
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Objective: Cytomorphological analysis requires manual microscopy scanning to determine whether the cells are malignant, benign or reactive. During manual microscopy diagnosis, firstly it is desirable from pathologists to provide the optimum focusing by moving microscope stage on the Z axis. After implementation of focusing, they must move the microscope stage on the 3D axes (X-Y-Z) without losing focusing to see all parts of the specimen in-focus. Hence, during manual screening that consumes a lot of time for cell identification, misdiagnosis may occur due to analysis of pathologists with poor concentration and short attention. In this study it is aimed to obtain a panoramic image with high resolution and all parts of the specimen in-focus.
Method: The proposed study consists of two main steps that are auto focusing and auto scanning. In auto-focusing step, an image with all parts of region in-focus is obtained with image fusion method based on wavelet transform. During scanning process, the images with overlapped areas are obtained with optimal auto-focusing and are used for image stitching.
Results: The results indicate that if in focus images that are obtained with image fusion are used for image stitching process the more feature points are produced, and panoramic image with higher resolution and more quality is obtained.
Conclusion: In this study, it is achieved to obtain a panoramic image higher resolution. Moreover, image stitching process is performed with loss of focusing and auto-focusing to show that autofocusing is crucial to obtain high quality panoramic image on microscopy.

PS-14-013
Identification of barriers and facilitators for the implementation of standardised structured pathology reporting in the Netherlands
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Objective: Standardized structured reporting (SSR) enables high quality pathology reporting. Although Dutch guidelines recommend SSR, uptake is relatively slow in the Netherlands. Identifying barriers and facilitators for SSR by pathologists is necessary to develop tailored implementation tools to increase SSR uptake.
Method: A focus group interview identified facilitators and barriers for SSR. These factors were classified by the theoretical framework levels of Flottorp: innovation (SSR), professional (pathologist), social setting, organization and (inter)national regulations. Findings were quantified using a web-based survey among Dutch pathologists.
Results: Ten pathologists participated in the focus group, and 92 pathologists completed the survey. Main barriers for SSR were inability to express nuances (30 %), and no clarity of usability (41 %). Barriers within the social setting were lack of support from direct colleagues (20 %) and the multidisciplinary team (34 %). At organizational level, lack of support by managers (11 %) and lack of information on availability and updates of SSR-modules (22 %) were mentioned. Facilitators for SSR were the SSR-module as a tool (72 %), and improved communication during multidisciplinary team meetings (80 %).
Conclusion: Barriers and facilitators for SSR exist at different levels. These factors will be used to develop tailored implementation tools to improve uptake of SSR in the Netherlands.

PS-14-014
Automated nuclei detection in pleural effusion based on machine learning
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Objective: Pleural effusion, accumulation of fluid in the pleural space, is frequently encountered specimen type in cytopathological assessment. Cytomorphological assessment, performed by pathologists under light microscope, reguires scanning all cells, determining whether the cells

are malignant, benign or reactive. Since this assessment is tedious, subjective, time-consuming and in many cases error-prone procedure, the need for automated microscopy systems is arised. The detection of cell nuclei is seen as the corner stone for diagnostic purposes in automatic analysis of cytopathological images. Because, the nuclei is most salient structure within the cell and it exhibits significant morphological features and changes which contribute in the discrimination of malign, benign and reactive cells. Identification of the cancer cells in pleural effusion cytology allows for the early diagnosis of the cancer and also the staging, prognosis and monitoring these cells.
Method: With the development of machine learning algorithms, medical image processing applications have adapted these algorithms to enhance medical image classification performance.
Results: The experimental results show that the detection of the cell nuclei by the machine learning method is highly accurate.
Conclusion: In this paper, we investigate the applicability of machine learning techniques to create a fully automated system for cell nuclei detection in pleural effusion cytology.

PS-14-015
MIAP - a new web-based platform to support the pathological diagnosis
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Objective: Design of a new web-based platform to support the pathological diagnosis for consultation, WSI analysis, collaboration between pathologists and scientists, create a research group and sharing the medical data.
Method: The MIAP platform is located in the server https://miap.wim.mil.pl of Military Institute of Medicine. The user can upload WSI with the histopathological description, shows it directly in Internet browser with the help of OpenSeadragon library, makes annotations, performs the quantitative analysis of the selected regions or whole specimen and presents graphical results on the WSI with the score sheet. The platform offers algorithms for Ki-67, ER and PR stainings in breast cancer and Ki-67 in brain tumours to research purpose. Additionally, a set of brain tumour and breast cancer cases are accessible for educational purposes and the user can share his cases for consultation.
Results: The developed MIAP platform has been intensively examined through the last year. A lot of user-friendly capabilities were added. The algorithm for the hot-spot selection and quantification in WSI is able to performed analysis in 2–3 min.
Conclusion: The presented platform offers the free tool for pathologists and scientists in digital pathology. This study was supported by the National Centre for Research and Development, Poland (grant PBS2/A9/21/2013).

PS-14-016
Linkage of the Dutch Pathology Registry to clinical registries and biobanks
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Objective: The objective of our study is to build a powerful and sustainable research infrastructure for requesting pathology data, corresponding tissue, other biospecimens, images and clinical data for research purposes. In this way we facilitate researches with easy access to research data and/or materials from different registrations. Our ultimate goal is to form part of a national infrastructure for personalized medicine&health research that will boost the quality and speed of translating proof concepts to implementation in clinical care.
Method: To integrate a generic request portal for requesting samples, images, and data within BBMRI-NL and to perform pilot linkage studies between the Dutch Pathology Registry (PALGA, including the Dutch National Tissuebank Portal) and other clinical registries and biobanks in the Netherlands.
Results: Pilot linkage studies were successfully performed between the Dutch Pathology Registry (including the Dutch National Tissuebank Portal) and the Netherlands Cancer Registry and PHARMO institute for drug outcome research, respectively. Linkages with Parelsnoer Institute (pearls: kidney failure, hereditary colorectal cancer, and inflammatory bowel disease), NefroData (kidney dialysis), GENCOR (familial heart diseases), and LifeLines (multi-disciplinary prospective population-based cohort study) are currently being explored.
Conclusion: Combining data and/or material from different registries and biobank to pathology data offers unique opportunities for scientific research.

PS-14-017
Simulation program for whole slide image (WSI) primary diagnosis
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Objective: The objective is to convince the conservative pathologists that recent WSI images are clear enough for primary diagnosis.
Method: We prepared about 60 WSI images of popular lesions from various organs. Rare cases or difficult specimens are avoided. We opened a website, and after registration, new pages showing 24 organs will open. If you select stomach for example, then 3 cases with simple clinical information and thumbnail of WSI images will open. After selecting cases, you can see WSI images with full operability. Then you will back to the thumbnail screen with diagnosis window where you can type your diagnosis. Clicking the answer button, you will see the answer with question asking the WSI image is 1) good enough for primary diagnosis; 2) I'd like to review by microscope, 3) too poor for primary diagnosis.
Results: Most of the pathologist selected the answer 1). Some of the WSI images were not clear enough due to technical problem which is easy to solve.
Conclusion: Many experienced pathologists are hesitating to make primary diagnosis by WSI images. This program may help to overcome the problem.

PS-14-018
Do snapshot and whole slide image analysis display with differences of Ki-67 stained invasive breast carcinoma specimens?
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Objective: To compare the DIA of the snapshots of the virtual slides with that of the WSI for Ki 67 assessment in invasive breast carcinoma specimens.
Method: A retrospective and prospective study including 100 patients diagnosed with invasive breast cancer. DIA of Ki67 was performed on both snapshots from the virtual slides & WSI.
Results: Comparing the Digital Image Analysis of the snapshots of the virtual slides with that of the WSI revealed that the results of DIA of the snapshots were more corresponding to the results obtained from optical microscopic examination and that from examination of the virtual slides on the monitor. A lot of falsies were detected in the results of the DIA of the WSI most probably due to the false results gained from areas of inflammation & necrosis in the slides.

Conclusion: Such study concluded that DIA of the snapshots obtained from the virtual slides is still the most accurate method for evaluation of Ki67 in the cases of cancer breast.

PS-14-019

Impact of a laboratory information system - integrated speech recognition system as part of digitisation in pathology departments

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Objective: Digitization includes not only the scanning process, but also the traceability of tissue samples and report management. In our opinion, this last point has been insufficiently studied. Currently, in our center, resource limitations, mainly human, have resulted in the task of pathology report editing to be assigned to the pathologist, with the consequent work overload related thereof. With the aim of achieving time optimization, a speech recognition system (SRS) was implemented.
Method: Two pathologists from our department, specialized in gastrointestinal (GI) pathology, were involved in the implementation of a Laboratory Information System (LIS) –integrated SRS (INVOX Medical Dictation, Vocali). With a preliminary training period of 2 weeks, a total of 60 GI pathology cases were randomly selected, with the intention of comparing the reporting time for both typing and dictation. Several abbreviations and shortcuts were established when using the SRS, including SNOMED CT automatic coding.
Results: The overall reporting time for the 60 cases was 95′36″ (1′ 36″/case) with the typing methodology, while for the SRS it was 42′ 57″ (43″/case).This meant a reduction in reporting time of 55.2 %. In addition, there was a standardization of the pathology reports, both for structured texts and those edited as continuous text.
Conclusion: A SRS can help pathologists optimize time in signing out cases, making them more efficient and cost-effective. Abbreviations and shortcuts allow reports to be more standardized, while avoiding typing errors. At the same time, this methodology implies a lower physical demand, as it is more ergonomic and reduces work-related musculoskeletal disorders. Implementation of SRS should be considered in the context of going fully digital.

PS-14-021

A model for simulation of glands on virtual slides

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Objective: Big Data revolutionized machine learning and facilitated new forms of automation. It is possible to use deep learning to perform object segmentation of images given large enough training sets. The automatic segmentation and analysis of glands in HE stained tissue slides could facilitate the detection of all types of glands and support quantification. But training data is scarce, because of the time consuming and error prone process of labeling data by pathologists.
Method: We aim to bridge the gap in training data by synthesizing simulated HE-slides (phantoms) of prostate and colon gland tissue. A complex model based on distances, distributions, geometrical shapes and statistical processes was created. Texture was simulated using a neural network.
Results: This model randomly generates phantoms based on the given parameters which allows the creation of images of different tissue types with varying gland forms and types.
Conclusion: A model for the description of glands was developed which can be used to supplement training data for machine learning applications or as a benchmark for algorithm development. The model was evaluated using the generated phantoms to train a neural model for image segmentation, by statistical comparison to real images and it was examined by pathologists.

Tuesday, 5 September 2017, 09:30–10:30, Hall 3
PS-15 Nephropathology

PS-15-001

Clinicopathological study of amyloidosis in renal biopsy

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Objective: This study characterizes the clinicopathological features of patients with renal amyloidosis.
Method: We reviewed slides and clinical data of all amyloidosis cases ($N = 62$) in renal biopsies between 2011 and 2016. Amyloid characterization was carried out by immunohistochemistry (A protein and TTR) and direct immunofluorescence (light chains k and λ). Amyloid deposition was classified by Congo red stain according to its quantity (none, mild and high) and localisation (glomerular, vascular and tubulointerstitial).
Results: Mean age was 60; 31 (50 %) were women. The most frequent clinical change was nephrotic proteinuria/syndrome [43 patients (69 %)]. Six patients (10 %) were HIV+. Amyloidosis breakdown by type was: AA — 27 cases (44 %); AL — 24 cases (38 %) [k chain — 2 (3 %); λ chain — 22 (35 %)]; ATTR cases — 6 (10 %); and undetermined — 5 cases (8 %). All cases had vascular deposits, 39 (63 %) of which were high quantity; 97 % cases had glomerular deposits [38 (61 %) high quantity], and 43 % had tubulointerstitial deposits [9 (15 %) high quantity]. Amyloid quantity was similar in the different types ($p = 0,33$).
Conclusion: Amyloidosis is mainly a disease of older individuals. AA and AL were the most common forms. Amyloid was mainly deposited in the vessels and glomeruli. There was no association between the quantity and the type of amyloid.

PS-15-003

Findings in percutaneous renal biopsy: 12-year experience

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Objective: To present our experience and outcome of percutaneous renal biopsies for the diagnosis of nephrological and systemic diseases.
Method: Consecutive 242 percutaneous renal biopsies, taken from 232 patients and performed over a 12-year period were retrieved from our files. Renal biopsies were studied by light, immunofluorescence and electron microscopy.
Results: The mean age of the population was 48,8 years (range 14–89; 95 females and 137 males). Clinical indications which lead to renal biopsy were: acute renal failure (ARF, 26,4 %), nephrotic syndrome (NS, 19,8 %), chronic renal failure (CRF, 19 %), proteinuria (18,6 %) and proteinuria-haematuria (13,6 %). Pathological diagnosis were: IgA nephropathy (19,8 %), lupus nephritis (9 %), glomerulosclerosis (7,8 %), diabetic nephropathy (7 %), membranous glomerulopathy (7,9 %), minimal change disease (7 %), vascular diseases (5,4 %), tubulointerstitial nephritis (5,4 %), vasculitis (3,7 %), mesangial glomerulonephritis (3,3 %), membranoproliferative glomerulonephritis (3,7 %), amyloidosis

(3,3 %), combined (2,9 %) and various (7 %). 25 cases with glomerular damage presented tubule-interstitial nephritis. Six (2,5 %) were insufficient for diagnosis.
Conclusion: Percutaneous renal biopsy is an important procedure for evaluating proteinuria, haematuria and renal failure, providing vital information for diagnosis, prognosis and management of nephrological and systemic diseases.

PS-15-004
Diabetic donor kidney biopsy: Histological findings and graft outcomes correlations
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Objective: Recently, kidneys from marginal donors, such as diabetic donors, are used to expand the donor pool. We presented a retrospective cohort study using data from "Centro Regionale Trapianti Emilia-Romagna" in diabetic donors from 2004 to 2015.
Method: 45 diabetic donor biopsies were analyzed; histological parameters and recipients' clinical data were correlated. Karpinski score and histological classification of diabetic nephropathy were evaluated, adding microaneurysms, hyaline droplets, hyalinosis of basement membrane of glomerulus and thickening of basement membrane of tubules, for a total of 14 histological variables.
Results: No statistical correlations were found among Karpinski Score, diabetic nephropathy, kidney function and proteinuria, albeit single histological parameters, such as increasing of interstitial fibrosis ($p = 0.007$) and thickening of basement membrane tubules ($p = 0.009$) were associated with graft duration. Vascular damage was associated to eGFR Cockcroft ($p = 0.012$) and creatininemia ($p = 0.008$) 1 year after transplantation. Kimmelstiel-Wilson nodules were correlated to proteinuria ($p = 0.028$) and acute rejection ($p = 0.036$); glomerulosclerosis ($p = 0.034$) and vascular hyalinosis ($p = 0.048$) with graft loss.
Conclusion: Diabetic donor biopsy required more complex histological parameters than Karpinski score and classification of diabetic nephropathy. Pre-transplant pathological evaluation should be extended in order to predict graft outcomes.

PS-15-005
Nephrotic-range proteinuria and hematuria in a patient with mesangial matrix thickening: An ultrastructural diagnosis
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Objective: Fibrillary Glomerulonephritis (FG) is a rare glomerulopathy with no known associated disease, which has a heterogeneous histology that can suggest some differential diagnosis. Membranous glomerulonephritis, membranoproliferative glomerulonephritis and other glomerulopathies with organized deposits (GOD), like amyloidosis, cryoglobulinemic glomerulonephritis and immunotactoid glomerulopathy, must be excluded.
Method: A 33-year-old man presenting minimal bilateral tibial swelling and father with proteinuria. Urine analysis revealed nephrotic-range proteinuria, leucocyturia and haematuria. Blood test showed total-protein decrease. Minimal-change disease, focal-segmental glomerulosclerosis or membranoproliferative glomerulonephritis were clinically suggested.
Results: Renal biopsy revealed 26 glomeruli with global-diffuse endocapillary proliferation, mesangial matrix, basement membranes and capillary loops thickening, cellular interposition, double contours and no extracapillar crescents or amyloid. Immunofluorescence showed granular positivity for IgG, IgM, C3, Kappa, Lambda and focal for IgA. Ultrastructurally, thickened glomerular capillary walls and mesangial matrix contained granular densities intermigled with randomly oriented 10-12 nm-diameter fibrils. The diagnosis was FG, raising the possibility of Fibrillary Glomerulonephritis with fibronectin deposits.
Conclusion: FG is clinically similar to many glomerulopathies with Nephrotic-range proteinuria and hematuria, histologically encompassing other GOD. Differential diagnosis must rule out presence of amyloid or inmunoglobulin deposits, and if negative, ultrastructural studies should be considered to make an accurate diagnosis.

PS-15-006
An unusual form of monoclonal gammopathy of renal significance: Cryocrystalglobulinemia related kidney injury
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Objective: As an important cause of renal failure, kidney involvement by monoclonal gammopathies can be a challenging clinical and pathologic diagnosis.
Method: A 53-year-old man without significant past-medical history applied to our hospital with sudden anuria and serum creatinine of 11 mg/dl, requiring hemodialysis. He had thrombocytopenia and anemia with schistocytes in peripheral smear. Immunoelectrophoresis indicated monoclonal IgG-lambda in his serum. Bone-marrow biopsy was unremarkable without atypia in the cellular components.
Results: First kidney biopsy revealed intravascular thrombi and focal cortical infarct, along with intraglomerular, intravascular, and intratubular hyaline globules reminiscent of crystalline deposits of cryoglobulin precipitates. Leukocytoclastic vasculitis was not observed. Deposits stained positive for IgG and lambda light-chain without reactivity for kappa. A diagnosis of renal injury induced by monoclonal cryoglobulins was forwarded after laboratory tests confirmed cryoglobulinemia in the patient who then underwent plasmapheresis. Repeat biopsy showed new occurrence of focal endocapillary and extracapillary proliferation despite decreased intravascular/glomerular precipitates.
Conclusion: Cryocrystalglobulinemia related to monoclonal gammopathy can present with acute and severe kidney disease without systemic manifestations. Cryoglobulins may provoke thrombosis and can lead to focal infarcts. Crystalline deposits should be hunted routinely in adult patients with acute kidney injury especially when thrombotic microangiopathy like picture is evident both clinically and pathologically.

PS-15-007
Renal dysfunction in Leishmaniasis and Chagas disease co-infection: A case report
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Objective: Visceral leishmaniasis (VL) is an endemic parasitic disease that is very frequent in Northeast Brazil and may cause acute kidney injury (AKI) and glomerulonephritis.
Method: We present the case report of a patient with VL diagnosis, which developed severe AKI requiring dialysis.
Results: A 48-year-old man presented hematuria, increased abdominal size and cutaneous and skin pallor. After 5 months, he presents disorientation and dyspnea on exertion. At physical examination he had: paleness of skin and mucous membranes, hepatosplenomegaly and lower limbs edema.A test for rK39 was positive and a bone marrow aspirate evidenced VL diagnosis. Renal Biopsy shows post-infectious rapidly progressive glomerulonephritis and immunofluorescence was positive for IgM, C3 e C1q. The patient developed severe AKI requiring dialysis.

After treatment with amphotericin B for VL, there was a partial recovery of renal function

Conclusion: This case shows the importance of the inclusion of post-infectious glomerulopathies in the differential diagnosis of rapidly progressive glomerulonephritis, since recovery with improvement of renal function may remove the patient from the need for renal replacement therapy with reduced morbidity and hospitalization time. Endemic diseases in our country, such as VL and Chagas disease may be investigated in cases of AKI and glomerulonephritis.

PS-15-008

Prevalence of anti-phospholipase A2 receptor antibodies in Egyptian patients with membranous nephropathy

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Objective: Identify M-type phospholipase A2 receptor (PLA2R) associated primary membranous nephropathy (MN).

Method: Out of 1300 native biopsies received from 2016 to 17, 120 were diagnosed as MN, out of which 64 were stained for aPLA2R by immunoperoxidase. Ten cases of Lupus (SLE) Class V, 12 of hepatitis C&B Virus MN (10 HCV + ve and 2 HBV + ve) were used as controls. Positive was determined as diffuse glomerular capillary wall staining.

Results: aPLA2R was positive in 76 % of the 64 idiopathic cases and in 5 cases of the control group (3 HCV, 1 HBV, 1 SLE). None of the clinical parameters showed significance difference but nephrotic range proteinuria in the aPLA2R + ve group was more (63 % vs 45 %). Histologically, Only mesangial matrix expansion was significantly different in the aPLA2R –ve group (33.5 % vs 10.5 %, $p = 0.04$).

Conclusion: aPLA2R tissue staining is a reliable and specific method to identify primary MN and should be done routinely in all MN cases even those identified as secondary on clinical basis.

PS-15-009

A rare form of glomerulopathy associated to dysproteinemia

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Objective: Glomeruli are usually target for anomalous protein deposition. Rarely, deposition of monoclonal IgG may originate a proliferative glomerulonephritis, that is similar to others immunocomplexes glomerulonephritis and requires monoclonality confirmation by immunofixation.

Method: Female, 60-years-old, with no relevant clinical background, admitted due to progressive peripheral oedema with 1 month evolution and acute kidney failure. Echography was normal. Ancillary studies showed hypoproteinemia, hypoalbuminemia, kappa light chains increase with a high kappa/lambda relation. Viral and immune markers were negative. Bone marrow had 2.5 % plasmocytes—99 % different from normal.

Results: Kidney biopsy had 7 mm, 22 glomeruli, and showed membranoproliferative glomerulonephritis (MPGN) phenotype. No amyloid and light chain deposits were seen. There was chronic interstitial nephritis and cylinder tubulopathy. Immunofluorescence revealed positivity for IgG and C3, with negativity for IgA, IgM and light chains. Fibrinogen was equivocal. Conjugation of findings suggested multiple myeloma (MM) diagnosis. Patient started chemotherapy and, due to renal function impairment, hemodialysis.

Conclusion: This case was an unusual association of MPGN and dysproteinemia. The exclusion of autoimmune and infectious causes, by serology, corroborates the monoclonal IgG deposits hypothesis, even rarer in association with MM.

PS-15-010

Fate of renal tissue procurement at bedside in times of shrinking pathology laboratory budgets

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Objective: Renal biopsy is the gold standard for diagnosis native and allograft kidney diseases. Academic centers use Tissue Procurement at Bedside (TPB) to ensure specimen adequacy; however, as cost-cutting policies are becoming priority in most laboratories, the usefulness of TPB is being questioned.

Method: We compared 120 renal biopsies collected during 2015 using TPB (group A) to 111 renal biopsies collected during 2016 when TPB was discontinued (Group B) for specimen inadequacy rates. Banff criteria for allograft pathology was used for specimen adequacy. The impact of inadequate specimens on final pathology decision-making, and the rate of post-biopsy hematoma were assessed and correlated to the number of passes during the TPB. Two proportions test and Fischer's exact test were used for statistical analysis.

Results: Comparison between inadequacy rates of Group B versus Group A showed statistical significance concerning 5 of the parameters studied for light, immunofluorescence and electron microscopy (p-value < 0.05).

Conclusion: Our results show that elimination of TPB service from the anatomical pathology laboratory practice has a negative impact on renal specimen adequacy and therefore on diagnosis, directly affecting both native and transplant biopsies. Anatomical pathology laboratories should be aware of the consequences of eliminating TPB when trying to cut back on laboratory budget.

PS-15-011

Lupus Nephritis after liver transplantation

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Objective: Renal dysfunction in liver transplantation (LT) recipients is not uncommon and glomerulonephritis (GN) is also reported. However, lupus nephritis is a rare complication after LT.

Method: We present the manifestations of LN in a 18-year-old girl who received a cadaveric liver transplant due to Alagille syndrome. After 13 years of LT, she developed nephrotic syndrome without other symptoms of systemic lupus erythematosus. The amount of proteinuria was 20 g/24 hrs. Antinuclear antibody was positive, but anti-dsDNA and anti-Smith were negative. The serum complements were decreased. Pulse methylprednisolone was given and the dosages of all immunosuppressive drugs were set. Her edema and hypoalbuminemia worsened. She then developed pneumonia and died owing to multi-organ failure.

Results: Diffuse endocapillary and mesangial proliferative GN was detected in the renal biopsy. A full-house pattern was documented under immunofluorescent examination. Electron microscopy revealed subendothelial, subepithelial and mesangial electron-dense deposits. The tubular basement membrane showed irregular thickening, splitting and accumulation of electrondense particles. These findings were evaluated as compatible with LN WHO class IV-G (A/C) and electron microscopic changes of Alagille Syndrome.

Conclusion: Heavy proteinuria, hypoalbuminaemia and severity of renal impairment in LT recipients are the most important clinical variables that prompted a decision to perform a kidney biopsy.

PS-15-013

Glomerulitis vs. endocapillary hypercellularity in post-transplant IgA nephropathy

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Objective: In the context of post-transplant IgA nephropathy (TxIgAN), glomerular endocapillary hypercellularity ('E') and glomerulitis ('G') denote glomerular inflammatory cell infiltration incited by immune complex-mediated glomerulonephritis and antibody-mediated rejection (AMR), respectively.
Method: We reassessed 40 renal allograft biopsy samples of 37 patients who have been described to have glomerular inflammation. The samples were categorized as 'E', 'G', or 'G and E', in patients who were diagnosed with TxIgAN between January 1992 and December 2016.
Results: Glomerular inflammation was described as 'E', 'G', or 'G and E' in 11, 11, and 18 biopsies, respectively. Peritubular capillaritis, peritubular capillary C4d staining, and/or glomerular basement membrane doubling were co-existing in 22 biopsies (1 'E', 7 'G', and 14 'G and E'), which was interpreted as concurrent acute or chronic active AMR. In 14 biopsies (9 'E', 1 'G', and 4 'G and E') which showed mesangial hypercellularity (n = 8) and/or crescents (n = 10) but without other features of AMR, glomerular inflammation was considered a part of TxIgAN. In four samples of acute T cell-mediated rejection, glomerular inflammation was not associated with any of the above features.
Conclusion: In overlapping cases of TxIgAN and AMR, histologic distinction between 'E' and 'G' is difficult and arbitrary. The presence of peritubular capillary lesions without glomerular crescents is supportive of concurrent AMR in patients.

PS-15-014

Tubuloreticular inclusions in peritubular capillaries of renal allografts

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Objective: Tubuloreticular inclusions (TRIs) are anastomosing networks of microtubules that are frequently found in autoimmune diseases and viral infections. In renal allografts, TRIs have been reported in glomerular endothelial cells in association with viral infections and donor specific antibodies (DSAs), but their presence in peritubular capillaries has not been explored.
Method: We collected seven cases with TRIs out of 148 consecutive renal allograft biopsies taken from Dec. 2015 to Dec. 2016.
Results: TRIs were present in peritubular capillaries in seven cases and were concomitantly present in glomerular endothelial cells in two cases. The diagnoses included polyomavirus nephropathy (n = 2), acute T cell-mediated rejection (ACR) (n = 1), combined ACR and antibody-mediated rejection (AMR) (n = 1), suspicious for ACR (n = 1), chronic active AMR (n = 1), and moderate tubular atrophy and interstitial fibrosis (n = 1). Six patients had recent or current viral infections (BK polyomavirus, hepatitis B virus, herpes simplex virus, and cytomegalovirus in two, two, one, and one case, respectively). DSA was positive in one case. Five cases had moderate to severe interstitial inflammation and four cases had peritubular capillaritis.
Conclusion: TRIs are not rare in peritubular capillaries. They are associated with various viral infections and their appearance seems to be related to peritubular capillary injury.

PS-15-015

Clinical and morphological spectrum of biopsy-proven kidney diseases in the elderly

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Objective: The limited number of kidney biopsies performed in the elderly can contribute to missed or delayed diagnosis in this age group. The aim of this study was to examine the spectrum of renal diseases and their clinical presentations in elderly patients undergoing renal biopsy.
Method: All native renal biopsies performed from January 2006 to December 2016 in patients aged ≥65 years were analyzed. Histological patterns and clinical presentations of renal diseases in patients aged ≥65–74 years (Group I) were compared with patients aged ≥75 years (Group II).
Results: Of the 1425 native renal biopsy specimens, 178 were performed in patients aged ≥65 years. 146 biopsies were performed in patients aged ≥65–74 years, and 32 biopsies in patients aged ≥75 years. The number of renal biopsies performed in elderly patients was increased from 3 in 2006 to 33 in 2016, respectively. The most common clinical manifestation in patients aged ≥65–74 years was nephrotic syndrome, whereas proteinuria and acute kidney injury (AKI) were the most common presentations in patients aged ≥75 years. The most prevalent glomerular diseases in Group I were amyloidosis (AG) and membranous nephropathy (MN). The leading glomerular disease in Group II was pauci immune glomerulonephritis (PIGN). Chronic interstitial nephritis and acute interstitial nephritis were more common in patients in Group II than in Group I.
Conclusion: The study revealed differences in the histological patterns and clinical manifestations of kidney diseases in patients aged ≥ 65–74 years in comparison with patients aged ≥75 years. The total number of elderly patients receiving renal biopsy increased yearly.

PS-15-017

Malignant tumours in patients with renal transplant: 20-year experience of a single transplant center

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Objective: A retrospective analysis of peculiarities of development of malignant neoplasms in patients after kidney transplantation receiving long-term immunosuppression
Method: In this study we evaluated incidence of malignancies observed among 718 renal transplant recipient with at least 6 months of follow-up. A total of 561 men and 257 women, mean age at transplantation 36,3 + 8,3 years were included.
Results: Thirty three out of 718 recipients (4,6 %) developed malignant neoplasia: 45,5 % of these were Kaposi's sarcomas, 12,1 %—cancers of the uterine cervix, 12,1 % cancer of the stomach, 12,1 % - basal cell carcinomas, 6,06 % - posttransplant lymphoproliferative disorder. There was no significant effect of either cyclosporine A, tacrolimus doses or OKT3/ATG on the incidence of the tumours. The median time from onset of end-stage renal failure (dialysis start) and from the transplantation to the diagnosis of the tumour make up 32 (16–161) and 23 (5–158) mouths, respectively. One renal transplant recipient suffered from multiple myeloma with aggressive course. Three patients diagnosed with renal cell carcinoma of the transplant: clear cell carcinoma, papillary carcinoma, mucinous adenocarcinoma via 264, 24 and 4 months respectively.

Conclusion: The importance of strict adherence to intensive monitoring transplant patients, which can detect tumours at an early stage.

PS-15-018

Changes in tubular epithelial cells and tubular basal membranes in primary glomerulopathies

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Objective: The tubular basal membranes (TBM) are composed of Collagen IV and are considered as part of the renal interstitium. The objective of the study was to determine the changes of the TBM and overlying tubular epithelial cells (TECs) in various primary glomerulopathies.

Method: We performed light-microscopic analyses on thirty renal biopsies with glomerulopathy and interstitial fibrosis exceeding 10 %. The formalin-fixed, paraffin-embedded tissue sections were stained with hematoxylin-eosin, PAS, trichrom Masson, silvermethenamine Jones, Collagen IV, Cytokeratin 7 and Vimentin, and the semi-thin sections from the same tissue samples, fixed in glutaraldehyde and embedded in epoxy resin, were stained with toluidine blue and periodic acid-Schiff silvermethenamine.

Results: The light-microscopy showed thickened TBM surrounding the atrophic tubules in the areas of fibrosis, also seen on the immunostaining with Collagen IV. The analyses of the semi-thin sections showed dissection of the TBM, with single mononuclear inflammatory cells dispersed between the TBM and TECs, as well as between the layers of the delaminated TBM. The TECs laying on thickened TBM were positive for Vimentin and showed loss of expression of Cytokeratin 7.

Conclusion: Our study confirms the phenotype variations of TECs and the change of TBM of atrophic tubules in areas of interstitial fibrosis in various primary glomerulopathies.

PS-15-019

IgG4 related interstitial nephritis: A case report

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Objective: A 41-year-old man was referred for evaluation of renal failure. Mikulitz syndrome since 2010, ulcerative colitis and hypergastrinemia is reported from his medical history. Investigations: Urine analysis-trace proteinuria without active sediments. Urea 165 mg/dl; Creatinine 9.81 mg/dl; ANCAs negative. Serology for HIV, HBsAg, and anti-HCV antibody were negative. Serum IgG4 were 1070 mg/dL.

Method: Renal biopsy: Light microscopic examination revealed severe diffuse plasmacytic interstitial infiltration and a minor component of mature lymphocytes with mixed immunophenotype CD3(+) and CD20(+). Significant extensive fibrosis was observed occasionally with subtle storiform pattern and coexisting glomerular and tubular atrophy. Immunofluorescence for IgA, IgG, IgM, C3, C4, C1q, Fibrinogen, Albumin, κ λ light chains revealed non-specific findings. Immunohistochemicaly polyclonal plasma cells were identified with presence of IgG4(+) plasma cells >10–30/HPF.

Results: Our patient fulfills the mandatory criteria of presence of more than 10 IgG4 positive plasma cells per high power field.

Conclusion: IgG4-related disease is now considered as a systemic disease that might affect any organ system, including kidneys, lymph nodes, and salivary glands, with progressively growing fibro-inflammatory lesions causing a mass effect. Diagnostic criteria were established as: IgG4 plasma level of >135 mg/dl and an IgG4/IgG plasma cell ratio of >40 % with >10 and IgG4-positive plasma cells per HPF.

PS-15-020

Renal disease - de novo glomeronephritis in patients after allogenic bone marrow transplantation

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Objective: The recognized renal problems in Hematopoietic Stem Cell Transplantation [HSCT] recipients are drug toxicity, radiation nephritis, infection, thrombotic microangiopathy, graft-versus-host disease (GVHD) and glomerulonephritis.

Method: Two male patients aged 22 and 41 years old respectively, who had previously undergone HSCT for hematolymphoid malignancy presented with nephrotic range proteinuria and features of the nephrotic syndrome underwent renal biopsy.

Results: Case 1 showed pathologic features of glomerulosclerosis in 45 % of glomeruli and coexistence of focal segmental glomerulosclerosis [FSGS – NOS variant] in 12.5 % of glomeruli. Membranous glomerulonephritis [MGN] stage I was seen in the second patient combined with glomerulosclerosis in 39 % of glomeruli and FSGS—NOS in 24.5 %. Concomitant tubulointerstitial nephritis was seen in both cases. Features of calcineurin inhibitor toxicity were not seen.

Conclusion: In both cases the findings were those of chronic kidney disease [CKD] associated with findings of FSGS or MGN respectively on pre-existing HSCT probably in the broader context of cGVHD nephropathy. In such cases it is often impossible to separate cGVHD per se or if prior therapy increases the likelihood of CKD. The glomerular diseases are described as individual cases cGVHD in the kidney. Renal involvement in cGVHD referred to 0.5–1 % of patients with HSCT and MGN is the most frequent pathology.

PS-15-021

Three cases of adult-onset tubulointerstitial nephritis and uveitis (tinu syndrome)

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Objective: We report three cases of acute tubulointerstitial nephritis with concomitant uveitis (TINU syndrome) in three adult women. This entity is an uncommon condition affecting mostly adolescent subjects and young women, described in 1975, whose etiology and pathogenesis are unknown.

Method: Three women 48, 59 and 70-years-old were submitted to renal biopsy, because of renal failure with elevated plasmatic creatinine level. All patients, 3–5 months before complained of eye pain and redness diagnosed as iridocyclitis resolved, after many recurrences, with local steroid treatment. Of note the first patient complained sacroileitis and Epstein-Barr virus infection, the second had an history of asthma and atopic dermatitis; the third woman was treated for hypertension. In two cases ANA test was positive.

Results: Renal biopsies showed an interstitial nephritis with diffuse lymphocytic infiltration with plasma cells, neutrophils and eosinophils, tubular atrophy and a slight expansion of mesangium. Immunofluorescences were negative. Two cases were treated with steroid, one was left untreated. All cases were resolved.

Conclusion: Our cases confirm that this entity may occur and have a favorable outcome in adults. The renal biopsy associated to clinical findings is diagnostic. The good clinical outcome and response to

steroid treatment seems to suggest an abnormal immunological derangement.

PS-15-022

Acute tubular necrosis in renal graft biopsy: A retrospective single center review

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Objective: Complication after kidney transplantation is often delayed graft function growing in incidence commonly caused by acute tubular necrosis (ATN) connected with risk factors such as: cold ischemia longer than 24 hrs, prior sensitization of retransplanted patients, type of dialysis before transplantation and donor comorbidities.
Method: To determine the incidence of ATN in delayed graft function in transplant biopsies and establish the correlation with cold ischemia, a retrospective study was performed. We analyzed clinicopathological data for 148 transplant patients in the period from 1998 to 2015.
Results: ATN was diagnosed in 45 patients (30.4 %), 51.1 % female and 48.9 % male usually treated with standard immunosuppression. Mean time of the delayed graft function untill the diagosis of ATN was 19 days. Isolated ATN was present in 27 patients (60 %), remaining (40 %) was associated with borderline (17.77 %) or acute cellular rejection (22.22 %). Significant difference ($p = 0.001$) was observed among the group of patients with ATN of the median time of cold ishaemia 18.40 hrs compared to patients without theese changes (median 15.20 hrs). Donor vascular changes were present in 20 % of patients.
Conclusion: ATN is the most common cause of the delayed renal graft function and associated with the duration of cold ischemia.

PS-15-023

Nephrotic syndrome caused by membranous nephropathy with solitary IgA deposition along the capillary wall

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Objective: Histologically, idiopathic membranous glomerulonephritis (MN) shows IgG deposition on glomerular basement membrane (GBM) occasionally together with C3. Secondary MN accompanies other immne globulins and complements. We experienced a patient of nephrotic syndrome (NS) with solitary IgA depositon on the subepithelium of GBM.
Method: [Case] A 78-year-old male noticed leg edema and admitted to our hospital on emergency because of NS. Renal biopsy was done 5 days later. After steroid therapy, the leg edema disappeared, however, small aount of proteinuria continues to date.
Results: <Pathological findings>The specimen contained 16 glomeruli, including 2 global scleroses. Mesangial area showed no remarkable changes. On PAM staining, spikes and bubling were noted. There were no endocapillary hypercellularity nor extracapillary lesion. Interstitial fibrosis and tubular atrophy were mild. The vessels showed sclerotic change. On immunofluorescence microscopy, IgA showed positivity on GBM, and IgM on mesagial area. IgG was negative. On electron microscopic examination, the glomerular basement membrane was diffusely irregular and there were small amount of deposits on the subepithelium, suggesting MN.
Conclusion: Glomerular lesion with prominent IgA deposition includes mainly IgA nephropathy, infectious disease, systemic lupus nephritis, IgA vasculitis. Since our case is not consistent with them, we discuss on its ethiology.

PS-15-024

Membranoproliferative glomerulonephritis associated with infiltration of B cell small lymphocytic lymphoma in kidney biopsy: A case report and review of literature

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Objective: Glomerular diseases have been known to be associated with neoplastic diseases. Membranoproliferative glomerulonephritis has been reported to occur in association with non-Hodgkin lymphoma but there is few data reporting the coexistence of glomerulopathy and lymphoma infiltration of kidney parenchyma in the renal biopsy.
Method: We report the case of 70-year—old male with small B-cell lymphocytic lymphoma (SCLL) presenting with acute kidney injury (AKI) and nephrotic syndrome (NS).
Results: The patient underwent the renal biopsy that showed membranoproliferative glomerulonephritis (MPGN), and diffuse lymphoma infiltration of the kidney parenchyma. Light microscopy showed accentuation of lobular architecture and increased cellularity in all glomeruli. Immunofluorescence study revealed fine granular staining for IgG, C3, lambda and kappa light chains along capillary loops and in mesangial areas. Electron microscopy showed subendothelial and mesangial electron dense deposits consistent with MPGN, type I. Immunostains demonstrates a predominantly B cell population of lymphocytic cells infiltrating renal parenchyma that lacked expression of CD5 and cycline D1. The patient treated with prednisolone and cyclophosphamide reached complete remission of nephrotic syndrome with complete restoration of kidney function. The patient is in remission during 17 years of follow up after initial chemotherapy treatment of lymphoma.
Conclusion: This case shows the importance of the renal biopsy in kidney impairment due to the lymphoma. It must be taken into consideration that clinical presentation of acute renal failure may be due to the direct infiltration of the kidney by malignant lymphoma cells.

PS-15-025

The first experience in the IgM nephropathy diagnosis in paediatric patients in Belarus

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Objective: IgM nephropathy (IgMN) is an uncommon variant of primary glomerulopathy with dominant mesangial immunoglobulin M (IgM) expression. Experience is needed in the diagnosis of these diseases.
Method: We studied 10 kidney biopsies with single or dominant mesangial IgM immunohistochemical expression. All biopsies were made in 2013–2017 at the Republic Center of Paediatric Nephrology and Renal Replacement Therapy in Minsk, Belarus. All the cases included were classified as primary glomerulopathy.
Results: The age of patients ranged from 3 to 16 years old, boys and girls there were 6 and 4 accordingly. Five patients were diagnosed with nephrotic syndrome. Two of these patients presented high blood pressure level and hematuria. There was hematuria with non-nephrotic proteinuria in the four remaining patients. The most frequent glomerular morphological finding was diffuse mesangial hypercellularity: in 8 of 10 patients. In two cases, focal and segmental glomerulosclerosis was found. All biopsies had diffuse mesangial positivity for IgM and in seven cases there were also focal and segmental deposits of the immunoglobulin A, G and/or C3, C1q complement fractions.
Conclusion: The clinical manifestations and morphological findings in paediatric patients with IgMN is highly variable and this question demands the further studying.

Tuesday, 5 September 2017, 09:30–10:30, Hall 3
PS-16 Neuropathology

PS-16-001
Histopathologic pattern of ependymomas at an African tertiary hospital
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Objective: To determine the histopathologic pattern of Ependymomas at the University College Hospital, Ibadan Nigerian over a seventeen-year period. Ependymomas make up 19.5 % of paediatric Central Nervous System tumours at our institution.
Method: H & E Slides of all patients with clinical and radiological features of intracranial space occupying lesions were reviewed over a seventeen-year period
Results: There were 31 histologically diagnosed cases of Ependymomas. 21 (67.7 %) were males and 10 (32.3 %) were females with a ratio of 2.1:1. Median age of the patients was 19.6 years. Age range spanned 10 months–60 years. Grade I (Myxopapillary) Ependymomas accounted for 3 cases (9.7 %), Grade II Ependymomas accounted for 17 cases (54.8 %) while Grade III (Anaplastic) Ependymomas accounted for the remaining 11 cases (35.5 %). Among the grade II cases, the tannycytic variant was the most common -16 cases (94.1 %). Only 1 case of the papillary variant which accounted for (5 %) of Grade II Ependymomas. Majority of Ependymomas were supratentorial in location (90 %), located in various areas including Cerebral parenchyma, Posterior Cranial Fossa, Thalamus. The remainder (10 %) were located infra-tentorially in the Conus Medullaris and Cervical Spine.
Conclusion: Ependymomas in our environment show a male predominance and involve mostly adult patients.

PS-16-002
A case of CNS embryonal tumour with rhabdoid features and preserved SMARCB1/INI1 and SMARCA4/BRG1 nuclear expression
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Objective: Atypical teratoid/rhabdoid tumour (AT/RT) is a malignant CNS embryonal tumour composed predominantly of poorly differentiated elements, frequently including rhabdoid cells. Most are associated with inactivation of SMARCB1/INI1 or SMARCA4/BRG1 genes. We present a case of a CNS embryonal tumour with rhabdoid features, with preserved SMARCB1/INI1 and SMARCA4/BRG1 expression.
Method: An 18 months-old male child was admitted with prostration, alimentary refusal and intolerance to being in prone position. On MRI, a large left supratentorial lesion was seen, with cystic-necrotic areas and calcifications. He was submitted to surgery.
Results: On histological examination, a highly cellular tumour of "small round blue cells" was seen with distinct rhabdoid cells. Areas of neuropil with ganglion cells and mesenchymal differentiation were also observed. However, on the immunohistochemistry, expression of SMARCB1/INI1 and SMARC/BRG1 were found to be preserved. At surgery, apparent total gross resection was thought to have been achieved and was followed by adjuvant radiotherapy and chemotherapy. Four years after surgery, the patient is alive, with no evidence of disease progression.
Conclusion: AT/RT is usually associated with loss of SMARCB1/INI1 or rarely SMARCA4/BRG1. Embryonal tumours with rhabdoid morphology and preserved expression of this genes are exceedingly rare. The presence of a component with ganglionic differentiation is also uncommon.

PS-16-003
Melanocytomas of the central nervous system: A short study of three clinically different cases and their histopathological particularities
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Objective: Primary melanocytic neoplasms of the CNS are rare tumours with reported incidence of about 1 in 10 million. Our study consists of 3 cases, diagnosed during a 1 year period, 2015 to 2016. We will try to empathise the similarities and differences of these three tumours regarding histopathological features as well as clinical presentation.
Method: The cases were diagnosed based on classical HE slides, correlated with neuroimaging and clinical data. Our results were later confirmed by immunohistochemestry.
Results: Three patients, two male and one female, aged 47, 63 and 26 were operated for tumours located in the craniospinal junction, pituitary and temporal lobe respectively. While the first patient presented location specific symptoms, the second had been diagnosed with a nonfunctional pituitary macroadenoma 14 years prior which was believed to have recurred. The third patient was being followed up for a thalamic cavernoma when a second lesion was observed. Histopathologically all tumours were heavily pigmented and, while the first presented an overall spindled morphology, the other two were epithelioid. While nuclear features were sometimes difficult to examine due to melanin deposits, none of the tumours had nuclear atypia or mitotic figures. The last case showed limited brain invasion but proliferation index remained low.
Conclusion: Though uncommon, melanocytic tumours affect a wide age range. Derived from leptomeningeal melanocytes, they usually involve the brain base. As benign tumours, prognosis is favorable yet the presence of certain features (the term "intermediate grade melanocytic neoplasm" was proposed) require close follow-up.

PS-16-004
Histiocytic spinal mass with Rosai-Dorfman immunophenotypic pattern in a patient with H-syndrome
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Objective: H-syndrome is a rare autosomal recessive multisystemic disease with clinical features including hearing impairment, hyperpigmentation, hyperglycemia, short stature, hypogonadism, hallux valgus and phalangeal flexure contractures and hypertrichosis.
Method: A 26-year-old Iranian boy with parents of a consanguineous marriage presented with progressive weakness of lower extremities since few months prior to this admission. On examination, Arcus senilis, bilateral sensorineurial hearing impairment, bilateral cervical lymphadenopathy, generalized cutaneous hyperpigmented plaques, hallux valgus and phalangeal flexure contracture in both upper and lower extremities and short stature (H: 157, Wt:37Kg) were noted. Past medical history was significant for Type 1/ Insulin-dependent diabetes mellitus which caused CKD and another removed histiocytic lesion on hand with pathologic diagnosis of histiocytic lesion. Thoracic and lumbospinal MRI showed a homogenous enhancing extradural soft tissue in thoracic canal (mainly T6-T8 level) with cord compression.
Results: In histolopathological examination, the lesion is composed of large histiocytes, some plasma cells, and scattered lymphoid aggregates. Immunohistochemical staining revealed positivity of histiocytes for CD68 and S100 and negativity for CD1a.

Conclusion: Rosai-Dorfman pattern is the most common form of histiocytosis in H-syndrome. To our knowledge, this is the first case of H-syndrome with CNS-histocytic involvement and the second case reported from Iran.

PS-16-005

Primary central nervous system lymphomas in immunocompetent individuals

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Objective: To study and categorise primary CNS lymphomas with emphasis on epidemiology, radiological findings, treatment and follow up .
Method: Retrospective descriptive study done from June 2010-December 2016 .
Results: During this period 1886 brain biopsies were received, of which 34 (1.8 %) were CNS lymphomas including 30 (1.6 %) primary and 04 (0.2 %) secondary lymphomas. The most common site for primary CNS lymphoma (PCNSL) was frontal region (34.4 %). The most common PCNSL was DLBCL accounting for 93 % with 28 cases of non-Germinal Centre (GCB) type. The unusual lymphomas were 01 case of plasmablastic lymphoma , 01 case of T-cell lymphoma and 01 case of CD 20 negative DLBCL and 01 case of cerebellar DLBCL. All the patients were immunocompetent with median age of 65 years. The contrast enhanced MRI brain findings were concordant in 20 cases (66 %). Out of all PCNSL , 11 are under follow-up, 04 are undergoing treatment while 03 patients died. Following treatment, 05 cases presented with relapse and 07 cases lost to follow up.
Conclusion: In various PCNSL, DLBCL is the most common and most aggressive of all lymphomas. PCNSL should be categorized on the basis of morphology and immunohistochemistry which helps in definite management at the earliest.

PS-16-006

Analysis of selected protein biomarkers in cerebrospinal fluid of neuropathologically confirmed neurodegenerative diseases

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Objective: The definite diagnosis of neurodegenerative diseases is possible only neuropathologically by confirmation of accumulation of pathologically conformed proteins characteristic for each neurodegeneration after the autopsy. Analysis of these proteins in the cerebrospinal fluid (CSF) of patients could help in clinical differential diagnostic procedure. In our study, we examined levels of selected CSF protein biomarkers in neuropathologically confirmed cases.
Method: We analyzed postmortem and antemortem collected CSF (n = 88) according to standardized protocols during the autopsy and clinical neurological examination in neuropathologically confirmed cases of frontotemporal lobar degenerations (FTLD-TDP), progressive supranuclear palsy (PSP), Alzheimer disease, Creutzfeld-Jakob disease (CJD) and mixed neurodegenerative diseases. Total-tau, phospho-tau, beta-amyloid, TDP-43 and progranulin CSF levels were measured and quantified using ELISA and statistically evaluated.
Results: In FTDL-TDP and PSP cases we found significant difference in CSF progranulin levels when compare to CJD cases. Difference in other evaluated markers were not significant.
Conclusion: For further development of diagnostic and prognostic biomarkers are autopsy-based biomarker studies essential. Protein biomarkers in CSF could be important for clinical diagnosis, treatment and prognosis of different neurodegenerations.

PS-16-007

Cerebral amyloidoma presenting with visual disturbance as leading symptom: A case report

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Objective: Amyloidomas are extremely rare in the central nervous system and most of them are primary confused with more invasive process in the brain. We present a case of 64-years-old female patient with episodes of Amaurosis fugax followed by painless transient monocular and binocular loss of vision for over a year.
Method: The patient was admitted with visual disturbances occurring on three consecutive days and lasting for about ten minutes. A follow-up MRI and diagnostic biopsy was performed. On selected samples fluorescence assay with Thioflavin-T, histochemical analysis with Congo red and immunohistochemical analysis with CD3, CD8, CD20, CD68, kappa and lambda immunoglobulin-light-chain were made.
Results: The histologic analysis revealed fragment of brain tissue with gliosis and intermittent masses of amorphous eosinophilic material with few scattered aggregates of plasma cells and lymphocytes. Additional analyses revealed congophilic material with Thioflavin-T-positivity characteristic of amyloid, few CD3 and CD8 positive lymphocytes and no CD20 positive cells. There was mild microglial activation with CD68 positive cells in the brain tissue as well as in the amorphous material.
Conclusion: Although extremely rarely encountered, primary cerebral amyloidomas need to remain in the differential diagnosis of patients presenting with a solitary or multiple intracerebral masses followed with visual disturbances as Amaurosis fugax.

PS-16-008

Study of the expression of part-time heparan sulfate proteoglycans in Alzheimer's disease

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Objective: A central pathological event of Alzheimer's disease (AD) is accumulation and deposition of cytotoxic amyloid-Beta peptide (AB) in the brain parenchyma. Heparan sulfate proteoglycans (HSPGs) are found associated with AlfaBeta deposits in the brains of AD patients. Part-time HSPGs include cell surface CD44 (isoform 3 is HS-linked), neuropilin, serglycin and TGFBR3.
Method: 7 different areas of 24 brains (6 controls, 6 low AD, 6 moderate AD, and 6 severe AD) were obtained. Transcriptional levels of Part-time HSPGs using RT-PCR and the expression of the protein using immunohistochemistry were centered on Braak & Braak areas and nucleus basalis of Meyner and cerebellum
Results: All Part-time HSPGs were expressed in every studied area of the control and AD brains. CD44v3 showed the lowest expression levels while serglycin showed the highest expression levels. Statistical analysis pointed out significant underexpression of CD44v3 and neuropilin in most of pathological areas. Furthermore, serglycin was significantly overexpressed in most of the cases. Immunohistochemically, serglycin and neuropilin were observed highlighting neurofibrillary tangles and neuritic plaques. Serglycin also pointed out amyloid angiopathy.
Conclusion: Our study has revealed alterations in the expression levels of three out four part-time HSPGs. Immunohistochemistry showed that

serglycin and neuropilin expressions correlated with Alzheimer's disease pathology.

PS-16-009

Sellar atypical teratoid/rhabdoid tumour in an adult patient with previous pituitary adenoma

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Objective: To report a rare case of sellar atypical teratoid/rhabdoid tumour (AT/RT) in an adult female.
Method: A 58-years-old woman with a remote history of prolactin secreting pituitary adenoma, pharmacologically treated, presented with intense headache, visual impairment and diplopia. CT and MRI scans revealed an inhomogeneously enhancing intrasellar and suprasellar mass with invasion of cavernous sinus. The tumour was removed with a trans-sphenoidal approach.
Results: Histological examination with haematoxylin and eosin showed a tumour consisting of rhabdoid cells with eccentric nucleus mixed to pale cells. At immunohistochemistry, tumour cells demonstrated consistent expression of vimentina and only focal positivity for keratins, EMA and GFAP and negativity for INI-1, WT1, and S100. Proliferation index valued with Ki-67 was 70 %. Histological and immunohistochemical findings were consistent with AT/RT.
Conclusion: AT/RT is an aggressive tumour mostly seen in paediatric age and extremely rare in adult patients. To date, few adult cases were reported in literature, only some of which were localized in the sella turcica. This report aids in promoting the awareness to the neuropathologists that AT/RTs should be considered in the differential diagnosis of malignant sellar lesions in adult patients.

PS-16-010

Understanding the increasing incidence of NETs: A true rise in incidence or just improved diagnostic methods?

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Objective: The purposes of this study were to analyze the incidence and morphological aspects of neuroendocrine tumours (NETs) for a proper understanding and diagnosis according to the latest WHO guidelines.
Method: We researched the archives of the Pathology Department at Emergency County Hospital "Pius Brinzeu" Timisoara, Romania for a period of 10 years (2005–2014).
Results: We have found 97 cases of IHC confirmed NETs with the following results: increased incidence per year (from 2 cases in 2005 to 23 in 2014); male cases (52 %) and female (48 %), mean age 61–70 (40 %), primary tumours (60 %) and metastatic (40 %), pure tumours (88 %) and mixed (12 %). Anatomic distribution results revealed gastrointestinal (36 %), cerebral (16 %), bones (7 %), breast (6 %) and less percentage in lung, prostate, uterus, ovary, bladder and skin.
Conclusion: This analysis shows that the incidence of NETs is growing over the years, possibly due to the important use of imunohistochemistry, the development of diagnostic techniques and increased awareness.

PS-16-011

Primary cerebellum anaplastic seminoma

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Objective: Extragonadal germ cell tumours are rare and comprise 2–5 % of all germ cell tumours. Seminoma, yolk sac tumour and mix germ cell tumours are few of the extragonadal germ cells tumours arising within the brain. Primery pure yolk sac tumour arising in the cerebellum is extremely rare. The second one is anaplastic seminoma associated with a very poor prognosis and hase been reported in less than 20.
Method: A 39-year-old otherwise healthy male presented with progressive headaches. Initial imaging reported a single mass occipital lobe. Tumour markers with alpha-fetoprotein, beta-human chorionic gonadotropin, and lactate dehydrogenase were not elevated. We used histological and Immunostaining methods for diagnosis.
Results: By histological examination there are following changes: Cells are large, round-polyhedral with macronucleus and sharp polymorphism. Immunostaining results: PLAP+, OCT4+, CK5-, CK7-, S100-, CD30-, CD117-,TTF1-,GFAP-, CD56-.
Conclusion: This case is presented for its unconventional presentation, rarity of occurrence, and difficulty in diagnosis. With tumour markers such as PLAP, OCT4, CD30, CD117, GFAP, S100, CK5, etc. and suitable results confirmed the presence of anaplastic senimona of cerebellum. This case adds to the increasing literature on the rare entity of this tumour.

PS-16-012

Study of primary neurodegenerative pathology associated with prion diseases

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Objective: Previous studies have described that the presence of a proteinopathy would facilitate the aggregation of other proteins of neurodegeneration. We aimed to study primary neurodegenerative pathology associated with Creutzfeldt-Jakob disease (CJD)
Method: 30 cases with confirmed CJD were study during the period 2010–2015 in the Brain Bank of the Basque Country (Álava node). The major proteins implicated in neurodegeneration (Tau AT8, alpha-synuclein, TDP43, and beta amyloid) were analysed by immunohistochemistry. Clinical data was also reviewed.
Results: Our database showed a mean age of 70.5 ± 8.5 years; an interval of duration of the CJD of 6.9 ± 6.5 months and a percentage of the MM1 subtype of 43.3 %. Sixteen cases showed associated proteinopathy (53.3 %). In addition, 43.8 % of MM1 CJDs had associated proteinopathy. Furthermore, a significant higher survival was observed in the proteinopathy associated group with an average survival of 9.2 ± 1.9 months ($p = 0.03$). Moreover, an statistically significant higher survival was found in the cases of CJD MM1 histotypes with associated neurodegenerative proteinopathy, with an average survival of 8.7 ± 1.7 months ($p = 0.042$).
Conclusion: The presence of CJD-associated proteinopathy showed a significant increase in survival for both the CJD cases and also specifically the MM1 histotype.

PS-16-013

Subcutaneous myxopapillary ependymoma masquerading as pilonidal sinus

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Objective: Myxopapillary ependymoma (ME) is a different variant of ependymoma. It rarely occurs outside of the central nervous system and present as a tumour of the skin or subcutaneous tissue. We present a case report of a 17 years old boy with a subcutaneous sacrococcygeal ME who was initially treated for the pilonidal sinus.
Method: A 17-year-old boy presented with a painless, subcutaneous mass located intergluteal fold. There was no other finding in physical examination. It was clinically diagnosed as a pilonidal sinus and the tract was excised.

Results: In gross examination, the specimen was a subcutaneous tissue measuring 5,2x4,2x4 cm partially covered by skin and measuring 4,5x1 cm. Serial sectioning revealed multilobulated, mass with myxoid cut surface measuring 4,5x4x3,5 cm. In histopathological examination, tumour showed the typical histological appearance of a ME and besides there was a pilonidal sinus.
Conclusion: Ependymomas account for only 5 % of all neurogenic tumours. ME's a low-grade intradural tumour of ependymal origin that slowly growing in conus medullaris and filum terminale. It's considered grade I of IV (WHO) at these sites. About 50 cases of ependymoma in extraspinal locations have been reported and the majority of them occur in the sacrococcygeal subcutaneous tissue or the presacral regions.

PS-16-014
Neuropathological effect of airborne exposure to formaldehyde in occupational exposure
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Objective: There are many scientific consensus that chronic exposure to chemicals may induce pathological conditions. Currently, the potential role of endogenous formaldehyde and increase of acetylcholinesterase into the pathogenesis of neurological dysfunction has been characterized. However little attention has been paid to relationship between formaldehyde exposure and acetylcholine signals.
Method: Cholinergic signals as a neuropathological effect of formaldehyde has been investigated in all workers of 4 melamine workshops at Tehran. Acetylcholinesterase activity was conducted using Elman method. Airborne exposure to formaldehyde was evaluated by the National Institute of Occupational Safety and Health 3500 methods.
Results: Cholinergic activity in exposed people was evaluated 27.59 (min-max; 1.83–308.09) IU/L which is higher than control groups significantly. All of airborne exposure to formaldehyde were lower than the Threshold Limit Value Ceiling (TLV-C) 0.3 ppm accepted by ACGIH. There are spearman correlation between occupational exposure to formaldehyde and acetylcholinesterase activity.
Conclusion: Our experimental finding reveal that the neurotoxic pathogenesis of formaldehyde depends on the cholinergic activity. It can be concluded that formaldehyde cause acetylcholinesterase activity enhancement which could be associated to cognitive dysfunction.

PS-16-015
Chordoid glioma of the third ventricle: Diagnostic pitfalls and differential diagnosis of chordoid tumours - case report
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Objective: Chordoid glioma was first described in 1998 and included in the WHO classification 2 years later. While very rare (about 80 cases reported) it seems to be confined to the third ventricle area, specifically the lamina terminalis of its ventral wall.
Method: A 57 years old man was admitted to our hospital showing signs of elevated intracranial pressure. MRI revealed a dense suprasellar mass of 48/38/32 mm which "pushed back" the third ventricle. It was interpreted as meningioma. A subtotal resection was performed.
Results: Grossly, the tumour appeared as a whitish solid mass with a glossy, mucinous surface. It was included in two blocks of paraffin and prepared for examination. The patient however developed postoperative complications and died soon after surgery. Light microscopy examination revealed a chordoid looking neoplasm which was initially diagnosed as chordoid meningioma. Reexamining the case raised certain questions as no clear meningothelial features were apparent. Several areas of limphoplasmocitic infiltrate with frequent Russel bodies as well as important associated gliosis (with numerous Rosenthal fibers and granular eosinophilic bodies) gave it away as a chordoid glioma.
Conclusion: Differential diagnosis of chordoid tumours usually involves chordoma, chordoid meningioma and chordoid glioma, the last one being the least frequent. While location seems very specific, the other tumours are also common in the suprasellar area and regular neuroimaging does not always distinguish exact origin. Chordoid glioma is often associated with high perioperative mortality due to its deep location and hypothalamic involvement.

PS-16-017
Rosette-forming glioneuronal tumour: A rare low grade neoplasm with distinguishing histological features
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Objective: The term "Rosette-forming glioneuronal tumour of the forth ventricle" was introduced to the 2007 WHO classification after being described 5 years prior. Since then it has been reported to other locations. It is a rare neoplasm and while incidence rates are still unavailable we found around 60 reported cases to date. We believe it to be more frequent but often misdiagnosed.
Method: A 15 years old male, treated for epilepsy, underwent a cerebral MRI. The scans revealed a relatively circumscribed, T2 hyperintense mass with moderate edema in the IV ventricle area. Neurosurgical resection was decided. During intraoperative examination, frozen sections and squash technique showed both glial as well as neurocitic elements.
Results: Examination of the parafin embedded, HE colored sections confirmed this biphasic pattern. The glial component revealed a loose, fibrilary matrix with few Rosenthal fibers and eosinophilic granular bodies. The neurocitic areas consisted of small cells with round nuclei arranged around a neuropil core which gave the distinct appearance of rosettes. Vascular proliferations were focally present as part of the glial, pylocitic-like component. No mitotic figures were present.
Conclusion: Our case represents a typical one: young adult with IV ventricle tumour showing byphasic glial and neurocytic patterns. Such patterns are very important to recognize as the tumour is grade I with very good clinical outcome. Our patient shows no postoperative deficits and will continue to be followed up. The presence of epilepsy was an unrelated condition.

PS-16-018
Dysembryoplastic neuroepithelial tumour - histological evolution: A case report
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Objective: A dysembryoplastic neuroepithelial tumour (DNET) is widely recognized as a benign mixed neuronal-glial tumour of children and young adults and classified as a WHO grade I tumour. However, there are 11 cases of malignant transformation reported in the literature. A histological evolution of a DNET case is presented.
Method: A 4-year-old boy with a 6 month history of seizures was referred to neurosurgery. Magnetic resonance imaging (MRI) revealed a lesion in the left frontal-temporal lobe. He underwent surgery and histopathological evaluation disclosed a typical DNET. Three years after the initial surgery, follow-up MRI demonstrated progression of disease. Reresection was performed, and the specimen was again interpreted as a DNET. Ten years later, the patient presented a new lesion at the base of the previous surgery which was again removed.

Results: Histopathological examination of the new lesion showed an oligodendroglioma WHO grade II, lacking IDH mutation and 1p/19q codeletion—paediatric-type oligodendroglioma.
Conclusion: Although the majority of DNET cases demonstrate benign behaviour, it retains the potential for recurrence and malignant transformation. The use of regular imaging examinations and the maintenance of a long-term follow-up is of importance, even after gross total resection.

PS-16-019
Lafora disease: A report of rare entity
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Objective: Lafora disease is the principal form of adolescence-onset progressive myoclonus epilepsy. There are only 200 reported cases in the literature. Our aims is to study the clinico-pathological features of this rare entity.
Method: We report a case of Lafora disease diagnosed in our department.
Results: Our case is a 24-year-old woman, who is diagnosed with Lafora disease since the age of 20. She had a sister who had the same disease and who died at the age of 40. The clinical features consist of progressive myoclonic epilepsy, visual hallucinations and cerebellar ataxia. The diagnosis was confirmed by an axillary skin biopsy that shows PAS positive inclusion in the cells of the sweet ducts.
Conclusion: LD is a rare autosomal recessive progressive myoclonus epilepsy due to mutations in the EPM2A and EPM2B genes .The diagnosis is suggested by the association, in an adolescent, of epilepsy, myoclonic seizures and progressive cognitive deterioration. The electroencephalogram is characteristic. The diagnosis must be confirmed by demonstrating Lafora bodies in histological examination. These bodies are composed of abnormal glycogen called polyglucosans . The evolution is often fatal .Genetic counseling are important and social support is essential in disease management.

PS-16-020
Alzheimer's disease, a consequence of microglia dysfunction?
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Objective: Alzheimer's disease (AD), the most common cause of dementia, represents a neurodegenerative disease related to aging. With aging, our immune system may initiate averse inflammation that may involve the systemic and central nervous systems (CNS). Microglia, the resident CNS macrophages, play a central role in AD. These cells regulate neuroinflammation in AD and are involved in disease propagation. They surround Amyloid-ß plaques, one of the pathological hallmarks of AD. Previously, using sera of the Rotterdam study, we identified the panprotease inhibitor Pregnancy Zone Protein (PZP) as a predictor for AD in women. PZP appeared to be elevated in microglia of AD patients. We want to compare the proteome of microglia of AD-patients with that of age-matched non-AD controls
Method: We stained fresh frozen postmortem brain tissue from AD patients and controls for P2ry12, a microglia specific marker. Using laser capture microdissection we enriched for microglia and analyzed the proteome using an Orbitrap mass spectrometer.
Results: This will allow us to specifically analyze the microglia proteome. Particularly in relation to PZP, which is also expressed by most P2ry12 positive cells.
Conclusion: The specific proteome of microglia of AD patients will aid in unraveling AD pathogenesis and reveal new ways to modulate AD progression.

PS-16-021
Detection of chromosome 1p36 deletion in primary cerebral neuroblastomas in adults
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Objective: to detect deletions in chromosome 1p36 in 3 cases of CNS neuroblastomas in adults.
Method: We studies cerebral neuroblastomas in 3 men aged 25, 54 and 59 years old, and 1 peripheral neuroblastoma in a six-month-old boy. The immunohistochemistry was performed using antibodies against CD99, GFAP, synaptophysin, EMA, pan-cytokeratin AE1/AE3, S100, vimentin, NSE, chromogranin A, p53 and neuroblastoma marker (clone NB84a); FISH analysis was used to detect 1p36 deletions.
Results: All CNS neuroblastomas and the peripheral one expressed S100, NSE, synaptophysin and did not express CD99 and the neuroblastoma marker. The average value of Ki-67 was 15–20 % in the adults and 52 % in the baby. The deletion in chromosome 1p36 was detected only in the patient aged 54 years with a slow-growing tumour for 6 years and the absence of recurrences and metastasis for 5 years after the treatment. In the other cases the tumours spread quickly, had large sizes, and the 25-year-old patient was twice diagnosed with recurrent neuroblastoma and re-operated.
Conclusion: A deletion in chromosome 1p36 was found in the adult patient aged 54 years, who had the most favourable outcome of neuroblastoma. The neuroblastoma marker expressed neither in cerebral nor in peripheral neuroblastomas.

PS-16-022
Recurrent pineocytoma-like papillary tumour of the pineal region (PPTR)
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Objective: We present a case of a patient with pineal region tumour with typical features of pineocytoma, which recurred after 7 years as a papillary tumour of the pineal region (PPTR).
Method: The analysis of clinical setting along with radiological and histopathological image lead us to the final diagnosis.
Results: In 2007, a 28 years-old male was diagnosed with a well-delineated 35 mm tumour in the pineal region with a strong, homogenous contrast enhancement both in CT&MRI scans. The tumour histopathologically consisted of solid and highly-cellular areas with small, uniform cells that formed typical rosettes. Atypia, mitoses and necrosis were absent. The tumour was positive for Synaptophysin, NSE, negative for GFAP. Ki67 index was 1 %. Considering the typical presentation, the tumour was diagnosed as WHO grade I pineocytoma. After 7 years, the neoplasm recurred and was composed mainly of papillary structures with cells with low-grade atypia. Rosettes, mitoses and necrosis were absent. The recurrent tumour was only focally positive for Synaptophysin, negative for GFAP, but it was positive for CKAE1/AE3 and CK18 which lead to the final diagnosis of a PPTR.
Conclusion: Our case shows that PPTRs can perfectly mimic pineocytomas. In such cases, staining for cytokeratins may lead to the correct primary diagnosis.

PS-16-023
Central liponeurocytoma of the supratentorial region: A case report of an unrecognised entity
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Objective: Liponeurocytomas are rare tumours, typically in a cerebellar location. They were found to have a characteristic cell of origin and mutations that lead to adipocytic differentiation. Extracerebellar locations of this entity have rarely been described.
Method: Thirty-four year-old woman presenting with headache and right hemiparesis in 2010. On MRI a left parietal tumour was found extending into the ipsilateral lateral ventricle and corpus callosum. She was submitted to surgery, the excision was incomplete and she suffered one local recurrence 6 years later. At this time she underwent radiotherapy and then reinterventioned.
Results: Microscopically, the neoplasia was solid and papillary, with psammoma bodies, formed by small isomorphic cells with rare dysmorphic nuclei; cytoplasm was vast, eosinophilic and finely granular. Cellular borders were indistinct. Foci of adipocytic differentiation were found. There were no mitosis, necrosis or endothelial vascular proliferation. A diagnosis of glioneural neoplasia with focal adipocytic differentitation was made, suggestive of supratentoral liponeurocytoma, grade two.
Conclusion: Supratentorial liponeurocytomas are a rare neoplasia, with morphologic peculiarities and a poorly established oncogenesis. Histological and immunohistochemical data which support our diagnosis are shown. The entity is not recognized in the latest WHO bluebook and further genetic studies are fundamental to better understand this entity.

PS-16-025
Loss of smarce1 expression is a specific diagnostic marker of clear cell meningioma: A comprehensive immunophenotypical and molecular analysis
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Objective: Clear cell meningioma is a rare grade II histopathological subtype that usually occurs in young patients and displays high recurrence rate. Germline SMARCE1 mutations have been described in hereditary forms of this disease and more recently in small clear cell meningioma series. The diagnosis value of SMARCE1 in distinguishing between clear cell meningiomas (CCM) and other meningioma variants has not been yet established. Our aim was to investigate the status of SMARCE1 in a series of CCM and its morphological mimickers.
Method: We compared the performance of an anti-SMARCE1 antibody and the molecular analysis of the SMARCE1 gene in a retrospective multicenter series of 10 CCMs.
Results: The loss of SMARCE1 expression was well-correlated with the presence of bi-allelic SMARCE1 alterations. Thus, we validated the anti-SMARCE1 antibody specificity by analyzing additional 300 meningiomas of various subtypes and 15 non-meningioma clear cell tumours by immunohistochemistry. Our series showed the loss of nuclear expression of SMARCE1 in all CCMs. In contrast, nuclear immunostaining was preserved in all other meningioma variants, as well as non-meningioma clear cell tumours.
Conclusion: Our series showed, for the first time, that SMARCE1 immunostaining is a highly sensitive biomarker for CCM, useful as a routine diagnostic biomarker.

PS-16-026
Prognostic significance of PD-L1 expression in glioblastoma
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Objective: The aim of this study was to determine the clinicopathological significance of PD-L1 expression in glioblastoma.
Method: The PD-L1 expression was determined using immunohistochemistry (IHC) in 115 glioblastoma patients. PD-L1 membranous staining more than 5 % of neoplastic cells in any intensity was considered as positive. Additionally, epidermal growth factor receptor (EGFR), p53, isocitrate dehydrogenase 1 (IDH-1) and CD3 expression of tumour infiltrating lymphocyte (TIL) was investigated by IHC.
Results: PD-L1 expression found in 37 (32.2 %) of 115 patients. Kaplan-Meier analysis indicated that PD-L1 expression was significantly associated with worse survival ($P = 0.017$). Also, PD-L1 expression was associated with a worse survival in grossly total resected group and grossly total resected with receiving both TMZ and radiotherapy group ($P < 0.05$). Moreover, the multivariate Cox analysis showed that PD-L1 expression independently predicted worse prognosis in grossly total resected group (hazard ratio (HR), 2.189; $P = 0.029$) and grossly total resected with receiving both TMZ and radiotherapy group (HR, 2.352; $P = 0.038$). PD-L1 expression was correlated with CD3 positive T cells infiltration and no expression of IDH1 ($P < 0.05$).
Conclusion: Our findings may yield improved responses to future immunotherapies and be helpful in predicting patients' outcome in glioblastoma.

PS-16-027
Immunonegativity for p16 as a poor prognostic factor in patients with glioblastoma: The experience of the GLIOCAT group
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Objective: CDKN2A is a tumour suppressor gene which encodes p16INK4a protein. The deletion of CDKN2A has been associated with a worse prognosis in patients with glioblastoma (GB). Our objective was to study p16 expression by immunohistochemistry (IHQ) in a GB series to assess whether it constitutes a prognostic factor.
Method: Using tissue microarrays we performed p16 IHQ in 276 GB cases in the context of a multicenter study (GLIOCAT). We evaluated p16 positivity on a semi-quantitatively scale from 0 to 5 as follows: 0 = 0 %; 1 = <5 %; 2 = 5−25 %; 3 = 25−50 %; 4 = 50−75 %; and 5 = > 75 % positive tumour cells.
Results: According to the aforementioned scale, 142 cases were rated as 0, 34 as 1, 27 as 2, 4 as 4, and 65 as 5. Kaplan-Meier curves showed significant differences in overall survival (OS) ($p = 0.017$, log-rank) among patients with GB having less than 5 % positive tumour cells (median OS, 15.3 months) and those with GB having more than 5 % immunoreactive tumour cells (median OS, 17.9 months).
Conclusion: In our hands p16 immunonegativity, defined as less than 5 % positive tumour cells, constitutes a poor prognostic factor in patients with GB.

PS-16-028
Eukaryotic initiation factors are altered in Alzheimer's disease
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Objective: Main neuropathological characteristics of Alzheimer's disease (AD) are amyloid plaques and neurofibrillary tangles formed by β-amyloid and TAU, respectively. This abnormal protein accumulation might occur due to dysregulated protein synthesis. One rate limiting step of protein synthesis is translation initiation regulated by eukaryotic initiation factors (eIFs). The aim of this study was to characterize the involvement of eIFs in AD pathology.
Method: eIF expression was analyzed on protein and mRNA level in two distinct murine AD models as well as in human post-mortem brain samples. Biochemical analyses were performed for hippocampal and cortical tissue of hTAU441 (V337M/R406W) mice as well as hAPPSL mice. In

humans, frontal and temporal cortical eIF expression was analyzed in grey and white matter.
Results: Cortical eIF4G expression was increased in APP overexpressing mice, whereas mice with elevated TAU levels revealed decreased eIF4G expression. In the temporal cortex of post-mortem AD brains, eIF4G and eIF4H protein levels were decreased in higher Braak & Braak stages. In frontal grey matter, eIF3 subunits were increased in AD patients compared to control subjects.
Conclusion: eIF levels are altered in human AD tissue as well as in murine AD models and might therefore be additional contributors to AD pathology.

PS-16-029
P16 overexpression supports the diagnosis of pilocytic astrocytoma
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Objective: Pilocytic astrocytoma (PA) is commonest paediatric glioma, grade I, with cell signalling activation but minimal proliferative activity. The main molecular alteration involves BRAF (tandem duplication and fusion with KIAA1549 in more than 70 %, BRAF-V600E mutation in 5 %). Previous studies have shown senescence phenomena in PA cell lines. The tumour suppressor protein p16 plays a role in the oncogenic-induced senescence. Our aim is to study p16 value in the diagnostic algorithm of PAs, mainly in the differential diagnosis with low grade diffuse astrocytomas (DAs).
Method: Forty-two PAs and 24 DAs were selected. P16 immunohistochemistry was performed. BRAF FISH study and BRAF-V600E PCR were performed in 30/42 and 17/42 PAs respectively.
Results: P16 expression was significantly higher in PAs than in DAs (p = 0,001) and in paediatric PAs compared to adult PAs (p = 0,012). P16 expression higher than 50 % had a PPV of 81 % in the diagnosis of PA. BRAF traslocation was found in 80 % and BRAF-V600E mutation in 5,8 %. P16 was overexpressed regardless of BRAF status.
Conclusion: P16 appears as a useful tool in the differential diagnosis of PAs and DAs, pointing towards PA when a strong expression is found. Oncogenic-induced senescence seems to have a different implication in adult and paediatric PAs.

PS-16-031
A case of diffuse midline glioma, H3 K27M-mutant
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Objective: Mutations of the genes H3F3A and HIST1H3B/C encoding the H3.3 and H3.1 histone variants characterize diffuse midline gliomas in children and young adults according to the recent WHO classification.
Method: A 23-year old female presented with early-morning headache, nausea and vomiting. The computed tomography revealed hydrocephalus and a hypodense region in the right basal ganglia and thalamus with no contrast enhancement. The magnetic resonance imaging showed a 4-cm mass with an ill-defined area of contrast enhancement. The patient underwent stereotactic biopsy.
Results: The neoplasm exhibited medium cellularity with mild nuclear pleomorphism and occasional large nuclei accompanied by high mitotic and ki-67 proliferation index (~50 %) but no necrosis or vascular hyperplasia. Immunophenotypically the cells expressed GFAP and p53, they were negative for the mutated proteins IDH1R132H and BRAFV600E, while ATRX expression was retained. Fluorescent in situ hybridization did not reveal EGFR gene amplification. The mutated protein H3.3 K27M (ABE419, Millipore, Billerica, MA) was expressed by all the neoplastic cells.
Conclusion: Diffuse middle gliomas harboring the H3 K27M mutation often exhibit aggressive behavior although cases of K27M-mutant low grade gliomas (pilocytic astrocytoma) have been described. The glioma of our case was markedly enlarged during the following months and was treated with radiotherapy and chemotherapy.

PS-16-032
View of tumours of the neurohypophysis according to the WHO classification of tumours of the CNS 2016: Case report
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Objective: The summary of diagnostic changes in chapter "Tumours of Sellar Region" in the WHO classification of tumours of the CNS 2016 with focusing on tumours of neurohypophysis. Case report.
Method: Comparison of classifications of tumours of neurohypophysis in the WHO classification of tumours of CNS 2007 and 2016. We focused on diagnostic changes, especially in using immunohistochemistry. Three types of tumours were described in the WHO CNS 2007: pituicytoma (PT), spindle cell oncocytoma (SCO) and granular cell tumour of sellar region (GCT). Tumour cells of pituicytomas strongly express the TTF1 like immature and mature pituicytes. It suggests their origin in pituicytes. TTF1 can also be detected in both SCO and GCT. This new fact supports their derivation from pituicytes too. The explanation of differentiation of three distinct tumours from pituicytes is the existence of several subtypes of pituicytes in physiologically developing neurohypopsysis.
Results: Based on new findings are three types of above described tumours now classified as variants of pituicytoma, WHO grade I. Our case represents mixed tumour of neurohypophysis derived from pituicytes.
Conclusion: Finding of parts of three distinct tumours of neurohypophysis in one unit is consistent with thesis of their common origin.

PS-16-033
Alexander's disease: A case report
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Objective: Alexander's disease (AD), also known as "fibrinoid leukodystrophy", is a progressive and fatal neurodegenerative disease. It's a rare genetic disorder caused by mutations in GFAP gene (17q21). It's inherited in an autosomal dominant manner; however, most cases arise de novo as a result of sporadic mutations. AD is characterized by delayed development of physical, psychological and behavioural skills, macrocephaly, seizures and spasticity; in some cases hydrocephalus, idiopathic intracranial hypertension, and dementia are present.
Method: 7-month-old male that required surveillance due to triventricular ventriculomegalia during prenatal screening. At 4-month-old he started with seizures that increased in frequency and became refractory to treatment. In posterior controls macrocephalia and psychomotor retardation were observed. MRI showed supra-infratentorial leukoencephalophathy.
Results: Post mortem histopathological study of the brain, brainstem and spine showed widespread astrogliosis, edema, fragmentation of the fibrillar matrix and extensive deposits of Rosenthal fibres in a diffuse and perivascular pattern.
Conclusion: The clinical and radiological suspicion of AD is confirmed by the histopathological study with destruction of white matter accompanied by the formation of fibrous, eosinophilic deposits, and the genetic

study, that showed heterozygous carrier c.716G>A (p.Arg239His) in the GFAP gene. There are less than 500 cases reported in the world.

PS-16-034

Subependymal giant cell astrocytoma with malignant features- a case report

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Objective: Subependymal giant cell astrocytoma (SEGA) is the most common, benign neoplastic process arising within the walls of lateral brain ventricles in patients with tuberous sclerosis complex (TSC), a genetic disease caused by inactivating mutation in the TSC1 or TSC2 genes.
Method: The patient at the age of 5 was admitted to the Neurosurgical Department. The brain MRI revealed multiple cortical and subcortical tubers and subependymal nodules, including an intraventricular tumour mass with a maximum diameter of 5 cm and features of hydrocephalus. The child underwent total resection of the tumour.
Results: Microscopic analysis revealed neoplastic tissue composed of large, gemistocytic, polygonal, occasionally multinucleated cells arranged in perivascular pseudo¬rosettes or sheets. The tissue revealed large areas of necrosis and proliferation of micro¬vessels. Mitotic figures were common, up to 5/10HPF, including atypi¬cal mitoses. The majority of tumour cells were strongly immunopositive for S100 protein, NSE and class III β-tubulin. Focal immunoreactivity was present for GFAP, neurofilament, Neu-N, synaptophysin, p63 and EMA. The EMA positivity was present in membrane and in cytoplasm as dot-like perinuclear or diffuse cytoplasmic immunoreactivity. The proliferative Ki67 labeling index was high, up to 25 %.
Conclusion: In conclusion, histopathological examination indicated atypical SEGA with anaplastic features and focal EMA immunopositivity.

PS-16-035

Embryonal tumour with multilayered rosettes: Two case reports of a rare tumour

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Objective: Embryonal tumour with multilayered rosettes (ETMR) is a rare entity, which was firstly defined in the 2016 by WHO.
Method: -
Results: Case 1: An 8-month-old girl was presented to the neurosurgery department with the symptom of severe vomiting. As MRI scan showed a contrasting irregular mass in the 4th ventricle, she underwent to tumourectomy surgery. Case 2: One-year-old boy with symptoms of intracranial pressure increase was admitted to the neurosurgery department. An excisional biopsy was performed because of non-enhancing mass which was detected in the parietal lobe posterior of central sulcus by MRI scan. Neoplastic cells, which had narrow cytoplasm and small blue hyperchromatic nuclei, frequently made multilayered rosettes, true rosettes, and pseudo-rosettes. In case 1, between the neuropilic areas, many rhabdoid cells were also noticed. Neoplastic cells showed immunoreactivity with vimentin, CD99, EMA(luminal), INI-1, and most importantly LIN28A. GFAP was positive in the neuropil areas. In case 1, desmin was positive in rhabdoid cells, respectively. The diagnosis was ETMR with rhabdoid differentiation, NOS, grade IV, for case 1. Diagnosis of case 2 was ETMR, NOS, grade IV.
Conclusion: ETMR is a rare, aggressive tumour of childhood. It contains poorly differentiated neuro-epithelium with neural, astrocytic,ependymal and even non-nervous differentiations. Rosettes, characteristic features of EMTR, may show different morphologies: Multi and/or mono layered, true and/or pseudo. Melanocytic, rhabdoid, and sarcomatoid differentiation have been reported in ETMRs. LIN28A immunoreactivity is an important diagnostic marker with high sensitivity and specificity for ETMRs. Differential diagnosis includes atypical teratoid rhabdoid tumour, medulloblastoma, and ependymoma.

PS-16-036

Extraventricular neurocytoma with atypical features: Report of one case with morphological, immunohistochemical and molecular findings

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Objective: To describe the morphological, immunohistochemical and molecular findings in one case of atypical extraventricular neurocytoma (AEVN).
Method: A 55-year-old male consulted because cognitive and motor disturbances. MRI showed a well-defined, 2.7 cm left frontal lobe tumour with contrast enhancement that underwent surgical resection.
Results: A highly-cellular, circumscribed neoplasm of monomorphous cells with round nuclei and well-defined cytoplasms with perinuclear halos organized in nests, ribbons and diffusely on a fibrillary background, with ganglion-like cells and rosette-like groups. Mitoses, foci of infiltrative growth and glomeruloid neovascularization were observed. Necrosis was not seen. Neoplastic cells were synaptophysin, CD56, NE, S100, Olig2 (patchy), p53 (10 %) positive and GFAP, EMA, CK negative. Molecular studies demonstrated co-deletion of 1p19q (82 %), IDH1 R132H mutation, metilation of MGMT promoter and absence of mutations of ATRX and BRAF. EGFR showed no amplification.
Conclusion: Despite the unequivocal neurocytic differentiation, our case showed some overlapping features with oligodendroglioma that made the diagnosis challenging. Although an infiltrative growth, 1p19q co-deletions and Olig2 expression have been described in AEVN, IDH1 or p53 mutations haven't been reported to date. These findings could support the existence of a distinctive glioneuronal tumour, a common progenitor cell with divergent differentiation and/or a histogenetic overlap between EVN and oligodendrogliomas.

PS-16-037

Two rare cases of kidney and lung cancer metastases to primary brain tumours

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Objective: Tumour-to-tumour metastasis (TTTM) is the uncommon phenomenon in the systemic and central nervous system neoplasia.
Method: We report two new cases of metastases to primary brain tumour. A 70-year-old man developed growing weakness in his left hand for the last 3 months; MRI of head revealed a parasagittal tumour. Three years earlier, he suffered radical nephrectomy on the right because of a renal cell carcinoma. A 68-year-old man underwent removal of oligodendroglioma (II WHO) 2 years ago. During the last year there was a gradual increase in neurologic symptoms; MRI revealed continued growth of the tumour, the patient underwent surgery for tumour recurrence.
Results: In the first case, histological examination showed a transitional meningioma (EMA, S100, PR were positive and CK AE1/AE3, CD10, RCC were negative) with areas of clear cell carcinoma (showed an expression of cytokeratin, CD10 and RCC, was negative for S100, PR). The diagnosis of transitional meningioma with metastasis of renal cell carcinoma was made. In the second case, histological examination revealed carcinoma metastasis to oligodendroglioma. The metastasis, consistent with lung cancer, was positive for CK7, TTF-1, napsin.

Conclusion: We have shown two rare cases of metastases to primary brain tumours.

PS-16-038

Determination of Indolamin-2,3-dioxygenase expression levels of diffuse gliomas and comparison of the results with the clinicopathologic data

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Objective: Today's treatment options of diffuse gliomas do not prevent adverse outcomes, especially in high-grade tumours. Immunotherapy has emerged as a new therapeutic approach in recent years and it is found to be that Indolamin-2,3-dioxygenase (IDO) which is a kynurenine metabolic pathway enzyme is playing a role in glioma cells immune escape and that high IDO expression levels are correlated with lower survival rates.
Method: This study included 82 patients with grade 2, 3 or 4 diffuse glial tumours according to WHO 2007 classification. All tumour sections were treated with IDO antibody and it is planned to record the percentage of staining and intensity (mild, moderate and severe) and to compare the results with clinicopathological data (tumour grade, age, sex, follow-up results).
Results: IDO immunoreactivity was not observed in any of our cases.
Conclusion: Consequently, we think that our study contributes to the literature when we consider that the IDO immunonegativity observed in our cases does not depend on the method of study or technical reasons and that the number of studies in this subject is low. However, in order to determine the location of immunotherapy in glial tumours, there is a need for a large number of studies also considering tumour heterogeneity.

PS-16-039

Neuropathology of opioid and stimulant drug abuse

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Objective: The use of illicit drugs is a serious medical, social and legal problem throughout the world. The most commonly used narcotics are from the groups of the opioids and stimulants.
Method: We examined a total of 4849 cases of deceased in the Department of Forensic medicine and deontology, Sofia, Bulgaria for the period 2011–2015. There of 146 of the cases had history of prolong drug abuse with opioids and/or stimulants. A histological examination was performed in order to determine the basic morphological changes in the brain tissue in drug addicts and compare them to a control group.
Results: Common finding were brain edema and acute venous stasis. The failure to comply with the basic principles of aseptic and antiseptics while injecting opioid drugs has led infectious agents, adulterants and unfiltered particles to enter the blood stream and cause damage to the brain and its vessels. In addition, thrombotic events and brain hemorrhages were present in individuals with evidence of stimulant abuse.
Conclusion: The central nervous system is the main anatomical and physiological target structure for different drugs. Based on the presented data the neuropathological alterations are mostly nonspecific, but they directly or indirectly play a role in the genesis of death.

PS-16-040

Proliferative activity (Ki-67) and level of VEGF gene expression in gemistocytic astrocytomas

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Objective: Gemistocytic astrocytoma (GA) is a rare variant of low-grade astrocytomas (GII), but some of them have a worse prognosis than other diffuse astrocytomas GII.
Method: 8 cases with GA were studied. Patients were aged from 31 to 72 years old. The material obtained during operations was subjected to histological, immunohistochemical (GFAP, Ki-67) and molecular genetic studies (VEGF mRNA expression was measured by RT-PCR).
Results: In patients with Ki-67 > 6 % (n = 6) proliferation of vascular endothelium was histologically identified and high/medium level of gene expression VEGF was identified by RT-PCR. In patients with Ki-67 < 6 % (n = 2) histological studies showed no vascular endothelium proliferation and VEGF gene expression level was low.
Conclusion: The proliferation of the vascular endothelium, Ki-67 > 6 % and high/medium levels of VEGF gene expression are more common in anaplastic astrocytomas. Therefore, some GA have the characteristics of astrocytomas GIII.

PS-16-041

Infantile desmoplastic ganglioglioma, a case report

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Objective: Desmoplastic infantile gangliogliomas (DIG) are rare and generally benign infantile intra-axial solid-cystic tumours, with a large size, clinical presentation of increased intracranial pressure, prominent benign desmoplastic structure on histology, and usually favorable clinical course. The low age of the patients, their low weight, and the large size of and the hyper-vascularized structure of the tumours are the main factors limiting surgery.
Method: Seven month-old girl with symtomatic partial epilepsy, whose MRI showed an expansive lesion in the right temporal pole, with a cystic component and a solid nodule that enhanced strongly with gadolinium.
Results: The leptomengingeal nodule consists of abundant desmoplastic tissue with a dense reticulin network that encircles the neoplastic neuroepithelial cells. Surrounding it, there is a less colagenized and more cellular interface composed mostly of primitive cells that co-express glial and neuronal markers. The proliferation index is low and the transition to the normal brain is well defined.
Conclusion: DIG are a key primary brain tumour to recognize in infants due to its commonly benign course. Although they are typically large with cystic component, the characteristic finding of a peripherally located enhancing nodule with a broad dural base can be helpful in differentiating DIG from infantile malignant primary brain tumours.

PS-16-042

Neuroblastoma of the brain

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Objective: Presentation of a case of a rare embryonal malignant brain tumour in a young adult
Method: The tumour involved the nasopharynx, posterior ethmoid and sphenoid paranasal sinuses, the anterior and the middle fossa and extended till the right cerebello-pontine angle. Two consecutive operations were made. The specimens from the two operations were received in formalin consisting of white and brown tissue fragments measuring 2X0,8X0,5 and 4,4X3,2X1,3 cm., respectively. H + E and immunohistochemical stains were conducted in order to identify the tumour

Results: The H + E examination from the specimen of the first operation revealed middle sized cells with basophilic cytoplasm, intense nuclear pleomorphism and diffuse pattern of proliferation. A lobular architecture and intermediate grade of nuclear pleomorphism was observed in the second specimen. A less dense cell population staining positive for S-100 was situated surrounding these cell lobules resembling a fibrillary matrix. The cells from the first specimen and the cells which were organised in lobules in the second specimen were immunohistochemically positive for NSE, chromograninA, synaptophysin, CD56 and b-catenin. Staining for LCA, p63, vimentin, CKAE1/AE3, GFAP, desmin, PgR, CD99, CD5, CD34 and EMA was negative.
Conclusion: Differential diagnosis between Central Nervous System neuroblastoma or esthesioneuroblastoma had to be made.

PS-16-043
An evaluation of brain tumour cases among Syrian refugees in Hatay, Turkey
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Objective: Cancer is of increasing importance in urban refugee populations. Among the refugees, such diseases are frequently neglected. Delayed applications lead to late detection of diseases. The tumours become too large and more aggressive, and so respond less to treatments. We aim to detect the frequency of brain tumour cases among Syrian refugees in Hatay, Turkey.
Method: In this study, 5484 Syrian patients, who underwent surgery and whose operation materials were sent to the Pathology Department, Mustafa Kemal University Research hospital, between 2011 and 2016, have been evaluated. 175 cases, who underwent surgery in the Brain Surgery Department, are analyzed.
Results: Of these 175 cases, 39 cases have been determined as non-tumoural , and 136 as tumoural. Statistically, the most common type is glial tumour (43 cases). %37.2 of the cases were detected at an advanced stage.
Conclusion: The civil war in Syria has forced many Syrian citizens to take refuge in Turkey, where treatment of cancer among refugee patients creates a massive burden on the health system. Therefore, it is of vital importance to take preventive measures and detect cancer cases at an early stage.

PS-16-044
An autopsy proven childhood-onset chronic traumatic encephalopathy
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Objective: An autopsy case of chronic traumatic encephalopathy (CTE) is presented.
Method: The patient was a 36 years old male. He had history of febrile seizures at 4 years old and had been severe mental retardation in his age of 10 when he was admitted to mental hospital. He had no clear history between the ages of four and ten. And suffered from repeatitive self-injury according to his hospital records.
Results: This case showed typical pathological features of CTE. The autopsy showed global brain atrophy including basal ganglia, thalamus, hippocampus, amygdala and mammillary and lateral geniculate bodies. There were phosphorylated tau positive neurofibrillary tangles (NFTs) and neuropil threads (NT), which were patchy and irregularly distributed throughout the brain, especially in deep sulci of neocortex. NFTs and NT were also found in basal ganglia, thalamus, amygdala and brainstem. b-amyloid deposit was rarely found only in motor and sensory cortex and a-synuclein was totally absent in the brain.
Conclusion: We report this case because it shows that autopsy findings can support the clinical history and diagnosis of CTE without a clear history of repeated trauma. This case also shows that CTE can occur in young ages and that even children can show the symptoms of CTE.

PS-16-046
An unusual metaplastic meningioma: Lipomatous meningioma
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Objective: Lipomatous meningiomas are extremely rare subgroups of meningiomas and are among the metaplastic meningiomas in WHO classification. It is characterized by the presence of fatty vacuoles between meningothelial cells. Lipomatous meningiomas do not require chemotherapy and radiation after total resection. Local recurrences can be seen.
Method: The surgical spesimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E.
Results: A 46-year-old woman admitted to the clinic with a history of seizures. MR showed a dural-based extraaxial mass lesion 18 mm in diameter in the right parietal posterolateral region of the brain. Microscopically, lipid vacuoles are observed among the meningothelial cells forming whorl structures and showing fascicular arrangement. Vimentin, EMA, SSTR2 and progesterone reactivities can be seen in the immunohistochemical study. Immunoreactivity of S-100 is present in lipid-laden vacuoles. Ki-67 proliferation index is between 2 and 3 %.
Conclusion: Meningiomas arise from the meninges-related arachnoidal cap cells and constitute about 15–30 % of the intracranial masses. They are benign, slow-growing and grade 1 tumours that are often seen in women in middle and older ages. Lipomatous meningiomas are characterized by the presence of lipid-laden cells. In conclusion, lipomatous meningiomas are thought to be lipidized meningiomas rather than true metaplasia by immunohistochemically and ultrastructurally. It is an uncommon tumour with favorable prognosis after total resection.

PS-16-047
Metastatic ductal breast carcinoma in meningioma: A case report
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Objective: Meningiomas and breast cancers statistically are very common tumours among women. However, metastasis from breast carcinoma into an intracranial meningioma is extremely rare. We present a case of 66-years-old female patient diagnosed with breast tumour on physical exam 2 years prior, but refusing further treatment at that time.
Method: After incidental fall from height the patient was admitted with vertigo and headaches. CT and MRI was performed which revealed temporoparietal extra-axial brain tumour measuring 7,4x6,3x4,8 cm and small diffuse post-contrast lesions suspicious for sarcoidosis. Surgery with fragmented excision and brain biopsy was performed. Gross examination showed hard white tumour parts with uniform cut surface. Standard procedure for histology and immunohistochemistry was made.
Results: Microscopically the tumour was composed of spindle-shaped fibroblastoid cells with small areas of edema. On one sample from totally fifteen taken and on the samples from the brain biopsy, micro-metastatic foci resembling ductal breast carcinoma were detected. Immunohistochemical positivity for CK7, E-cadherin, ER, PR and strong HER with high Ki-67, confirmed the diagnosis.
Conclusion: Tissue sampling plays great role in macroscopically undetectable lesions and patients without desire for cooperation. It is important

to avoid overlooking the diagnosis of metastatic disease, taking into consideration the requirements for specific treatment strategy.

PS-16-048

BRAF V600E-mutated brain tumour in an adult patient

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Objective: Introduction: Pleomorphic xanthoastrocytoma (PXA) is a rare brain tumour predominantly affecting children and young adults. PXA has a relatively favorable prognosis compared to infiltrating astrocytomas.
Method: A 49-year-old male presented with headache, nausea and cognitive affliction. MRI showed a tumour in the left hemisphere of the brain in the temporal-occipital region with the characteristics of high-grade glioma.
Results: Discussion: Based on the morphological appearance of the tumour, one of our first impressions was that of an epitheloid glioblastoma. In the immunohistochemistry the tumour cells are strongly CD34, S100, and Vimentin and partly GFAP and EGFR positive. Anti-p53 reveals only a faint expression in the tumour nuclei, ATRX is not lost. There is no expression of mutant IDH1. The MIB1 proliferation shows up with a maximum of 9 %. Based on the morphological appearance of the tumour, the first impressions was that of an epitheloid glioblastoma, however, due to the leptomeningeal growth, the presence of reticulin fibers, and strong CD34 immunoreactivity of tumour cells, we considered in our differential diagnosis also a pleomorphic xanthoastrocytoma (PXA).
Conclusion: Three months latter the patient presented new symptoms, CT-scan and MRI revealed a relapse of the tumour. After surgical resection we changed our diagnosis in epithelioid glioblastoma.

PS-16-050

Intracranial extraaxial anaplastic ependymoma: A rare localisation

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Objective: Intracranial ependymomas typically originate from ventricular system. Extra-axial, extra ventricular localization is not common. Extra-axial supratentorial ependymomas (EASE) are radiologically mimicking to meningiomas. There are several hypothesis about the origin of EASEs. The most favored one is that the tumour arises from heterotopic placement of ependymal cell rests during the fetal development and grows up subsequently.
Method: Twenty-seven years old female was presented to our hospital's neurosurgery clinic with complainings of hedache, vomiting and seizure. Cranial MR imaging revealed an extra-axial mass at right temporal region which was thought as meningioma preoperatively.The tumour was totally excised by left temporal craniotomy.
Results: The mass was in pale yelow and smoother than meningioma. The mass was attaching to dura mater. Histological analysis of the surgical specimens revealed perivascular pseudorosettes, atypic mitoses, necrosis and immunoreactivity for glial fibrillary acidic protein established the diagnosis of anaplastic ependymoma.
Conclusion: Although there are very few cases of supratentorial extraaxial ependymoma in the literature, it is possible to find it as it is in our case, and it should be kept in mind even though it is rarely seen in the differential diagnosis.

PS-16-051

Calvarial metastasis as clinic presentation of renal cell carcinoma: A case report

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Objective: Renal cell carcinoma (RCC) accounts for 2–3 % of all adult malignancies and 85 % of malignant renal tumours. Approximately 25 % cases of RCC present with distant metastasis at the initial evaluation. Renal cell carcinoma can metastasize everywhere, the most frequent sites are lung, bone, controlateral kidney. Calvarium is an extremely unusual site for a metastatic RCC.
Method: A 76-year-old male patient presented with enlarging mass, headache and tinnitus. Computerized tomography was performed, showing an expansive mass at subcutis, retroauriculer region up to talamic region.
Results: The mass was removed and it sized 6x5x2 cm. H&E stained sections revealed a malignant tumour arranged in papillary and nesting patern with variably sized tumour cell, nests were seperated by delicate fibrovascular septae. Cells in the larger nests were focally discohesive, giving rise to alveolar pattern. The tumour cells were large, round to polygonal, containing abundant, eosinophilic, and granular to clear cytoplasm. Mitoses were rare. The tumour cells were immunreactive for Vimentin, PanCK, EMA and CD10.
Conclusion: Renal tumours are frequently accompanied by bone metastasis. However few cases have been described of metastases occurring in the scalp. RCC should be part of the differantial diagnoses of growing lesions in the head and neck.

PS-16-052

Oligodendroglioma vs diffuse astrocytoma: Differential diagnosis of a LGG

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Objective: Low Grade Gliomas(LGG-WHO grade II) include astrocytoma, oligodendroglioma and oligoastrocytoma. Oligodendroglioma (median survival 12 years) presents low mitotic activity, no necrosis and the characteristic chromosomal codeletion 1p/19q. Diffuse astrocytoma (median survival 6–8 years) is a diffusely infiltrating neoplasm with hypercellularity, without mitoses. By imaging both neoplasms present diffuse infiltration with indistinct borders. Histologic diagnosis of a LGG is necessary, since it is related to prognosis for survival and prediction for response to therapy.
Method: Woman, 58 years old, came with bipolar disorder. CT: a low-grade lesion of 0,8 mm at left frontal-parietal lobe. MRI: lesion consistent with low-grade diffuse astrocytoma without calcifications. Paraffin-embedded tissue was examined with histochemistry, immunohistochemistry and in situ hybridization with MLPA.
Results: Microscopically, a low cellular tumour, consisting of monomorphous cells with round nuclei and often perinuclear haloes, was observed. No calcifications, no necrosis. Low mitotic count (1 mitosis/10HPF). Immunohistochemistry: GFAP(+), Leu-7(+), p53(10 %), Ki-67(4–5 %). Molecular testing: 1p/19q codeletion. Diagnosis: Oligodendroglioma WHO grade II.
Conclusion: Oligondrogliomas with 1p/19q codeletion have usually a retarded progression and a better response to chemotherapy. Since anaplastic transformation of a diffuse astrocytoma is higher than for oligodendroglioma, genetic testing for 1p/19q codeletion seems essential to incorporate to diagnosis so as to possibly direct treatment.

PS-16-053

Intracranial benign cystic lesions

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Objective: Intracranial cystic lesions are rare lesions and there is not yet a classification that includes all cystic lesions. In this study, we aimed to

investigate intracranial cystic lesions that underwent pathologic examination.
Method: Between 2010 and 2017, reports of 357 pathologic examination which were sent by neurosurgeons were retrospectively reviewed and 15 pathologically benign cystic lesions were detected. The histopathological diagnosis, demographic data and localisations of these lesions were evaluated.
Results: The most common diagnosis was epidermoid cyst (53.3 % (8 patients)). Others were cyst hydatid 20 % (3 patients), colloidal cyst 13.3 % (2 patients), enteriogenous cyst 6.6 % (1 patient), and glioependent cyst 6.6 % (1 patient) according to the order of frequency. 60 % of the cases were female, 40 % were male. The average age was 28.8 (standart dev.: 24). The most common cysts in children (0–18 years) were hydatid cysts, the most common in adults (> 18 years) were epidermoid cysts. Hydatid cysts and colloidal cysts were supratentorial and others were infratentorial.
Conclusion: While epidermoid cysts should be kept in mind in infratentorial cystic lesions in adults in preoperative evaluation, hydatid cyst should be suspected in childhood, especially supratentorial cyst in endemic regions.

Tuesday, 5 September 2017, 09:30–10:30, Hall 3
PS-17 Paediatric and Perinatal Pathology

PS-17-001
A rare paediatric case of the cholesterol granuloma in the maxillary sinus
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Objective: Cholesterol granuloma(CG) is usually associated with chronic middle ear disease,it's a rare histological entity in the maxillary sinus consisting of granulation tissue in which dense masses of cholesterol crystals and provoke foreign body giant cell formation.It's more common in middle-aged patients. We report a paediatric case of CG in the maxillary sinus,underlining the rarity and the differential diagnosis.
Method: A 12-year-old girl complained of chronic nasal obstruction and headache.Sinus endoscopy revealed a polypoid mass, and enlarged adenoids in the nasopharynx.Preoperative diagnosis was sinonasal polyp.Polypectomy and adenoidectomy were performed.
Results: Gross examination showed polypoid mass measuring 2x1,4 cm which had a tan-brownish appearance. Microscopic examination of the mass demonstrated tissue lined by respiratory epithelium with large numbers of subepithelial cholesterol clefts.Many histiocytes and multinucleated foreign body giant cells surrounded the cholesterol clefts. Focal areas showed degenerated red cells,hemosiderin-laden macrophages,lymphoplasmacytic cells,fibrosis and mucosal edema.Adenoidectomy material was reported as adenoiditis and lymphoid tissue hyperplasia.
Conclusion: Etiological causes has been suggested of maxillary sinus CG:disturbed ventilation,impaired drainage and hemorrhage into the sinus with hemolysis and accumulation of cholesterol from red cell membranes.The mode of therapy is surgical excision. Differantial diagnosis of CG should contain inflammatory/allergic polyps, mucoceles,sinusal cysts and tumours.Histopathologic analysis is necessary for the final diagnosis.

PS-17-003
Brain metastasis of a clear cell sarcoma of the kidney: A case report and review of the literature
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Objective: To report a case and review the literature.
Method: The MRI of a 16-months-old male child presenting with seizures revealed a lesion at the posterior fossa invading the 4th ventricle. At 2 months of age, he was diagnosed with a Clear Cell Sarcoma of the Kidney (SIOP stage IV – with axillary lymph node and cutaneous metastases) and treated according to a protocol for paediatric high risk renal tumours, with good response. Almost at the same time bone metastasis were identified.
Results: The histopathological examination of the brain lesion identified a neoplasm composed of uniform, small round cells with a clear appearance, separated by a delicate vascular network, one of the patterns observed in the primary tumour. The neoplastic cells were imunoreactive for Vimentin, Bcl2 and INI1; as in the renal tumour.
Conclusion: Clear Cell Sarcoma of the Kidney is an uncommon renal neoplasm of childhood. It's one of the tumours with most unfavorable prognosis, with high propensity to metastize to unusual sites. Brain metastasis have only infrequently been published.

PS-17-004
The spectrum of cloacal dysgenesis in one male and three female fetuses: Case study and review of the literature
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Objective: To describe features of cloacal dysgenesis, and emphasize on the extremely rare occurrence of cloacal dysgenesis in males, which may be prenatally misinterpreted as megacystis.
Method: We reviewed the postmortem findings and the prenatally detected ultrasonographic findings of four cases of cloacal dysgenesis in one male and three female fetuses. Fetal autopsies were carried out at the Department of Pathology of the National and Kapodistrian University of Athens, Greece. Our observations were compared with a review of the literature on cases of cloacal dysgenesis.
Results: All 4 fetuses showed a persistent cloaca (large dilated intraabdominal cystic formation, communicating with the intestine). Abnormalities or complete absence of the external genitalia and associated renal malformations were features noted in both female and male cases. The gonads were hypoplastic, absent or ectopic in one of the female cases. Anal atresia was present in all female fetuses, but was not seen in our male case. Vertebral defects were seen in one of the female fetuses. Cardiovascular malformations and focal amyoplasia were seen only in the male fetus. On prenatal ultrasonography all four cases were diagnosed as cases of megacystis. Dysplastic cystic renal changes were also detectable by ultrasound. Our findings were overall consistent with those described in the literature. Tubular hypoplasia of the aorta and focal amyoplasia of the intestinal wall have not been previously described in other female or male fetuses with cloacal dysgenesis.
Conclusion: According to our observations, megacystis detected in male fetuses on prenatal ultrasound examination may harbor the severe spectrum of cloacal dysgenesis, which necessitates a totally different parental counseling and therapeutic approach.

PS-17-005
Primary endocardial fibroelastosis in an infant with the prenatal diagnosis of dilated cardiomyopathy
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Objective: Endocardial fibroelastosis is thought to be a nonspecific reaction against hemodynamic stress, regardless of etiology. It may be classified as primary (idiopathic) or secondary, when in association with congenital heart diseases or viral myocarditis.

Method: We will report the case of a 78 day-old female infant (37 week gestation) with dilated cardiomyopathy and severe heart failure submitted to heart transplant. The diagnosis was established prenatally. No history of viral infections, metabolic disorders or family history of cardiomyopathies was known.
Results: Macroscopic examination of the explanted heart revealed a globular heart (47 g) with a dilated right ventricle and a pearly white plaque thickening of both ventricles. No other structural abnormalities were noted. Histological analysis revealed diffuse thickening of the endocardium, in both chambers, composed of parallel layers of collagen and elastic fibers. There was also vacuolization of subendocardial myocytes. These findings were diagnosed as endocardial fibroelastosis.
Conclusion: Cases in which no other cardiac abnormalities are found and the thickening process is diffuse are commonly referred to as primary endocardial fibroelastosis. Our case falls into this category. The diffuse involvement of both ventricles and the association with right ventricular enlargement has been rarely reported.

PS-17-006
Placental pathology varies in hypertensive conditions of pregnancy
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Objective: To retrospective correlate the clinical and placental phenotypes in various types of hypertensive diseases of pregnancy.
Method: 24 clinical and 50 placental phenotypes of ≥20 weeks pregnancies were statistically compared (ANOVA or Yates Chi-square with 5df and Bonferroni correction for multiple comparisons) among 91 cases of gestational hypertension (GH), 187 cases of mild preeclampsia (MPE), 211 cases of severe preeclampsia (SPE), 84 cases of HELLP or eclampsia (HELLP), 127 of chronic hypertension (CH), and 55 cases of preeclampsia superimposed on chronic hypertension (PCh).
Results: Statistically significant differences (p Bonferroni < 0.00172) separated GH and CH featuring the highest perinatal mortality (particularly macerated stillbirths), and acute chorioamnionitis (particularly maternal inflammatory response), from MPE, SPE, HELLP, and PCh showing the highest percentages of cesarean sections, decidual arteriolopathy, patterns of diffuse chronic hypoxic injury (particularly uterine), and villous infarctions. SP, HELLP and PCh featured the shortest gestational age at delivery, and CH and PCh the lowest percentage of clusters of maternal floor multinucleate trophoblasts.
Conclusion: Despite significant overlap, the findings show progression of features of placental malperfusion and shallow implantation from GH, through mild PE, HELLP to SPE (superimposed or not), indicative of the spectrum of same pathological process in PE of various severity, but not in CH.

PS-17-008
Expression miR-519, miR-17, miR-181a, miR-210 in placenta tissue in cases of early- and late onset preeclampsia
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Objective: The aim of the study was to evaluate localisation and expression in placenta villi miR-519a, -181a, -210 and -17 in cases of early–(EPE) and late – onset (LPE) preeclampsia.
Method: Groups with PE included 5 women with EPE and 5—with LPE. Control groups included 4 women with normal pregnancy (late control–LC), 38–39 gestation weeks, 4 samples—26–30 weeks (early control–EC). By hybridization in situ (Exicon, USA) was performed on 18 formalin-fixed paraffin-embedded placenta tissue specimens after cesarean section. The intensity of immunohistochemical reaction was estimated by means of Nikon Eclipse microscope imaging software (NIS-Elements).
Results: All miRs were determined in cytoplasm and nucleus of syncytiotrophoblast, stroma cells of placenta villi, syncytial knots, invasive trophoblast, decidual cells in LC. Expression of miR-519a, miR-181a in EPE predominantly was negative in all structures, but in LPE their expression was higher. MiR-519a, miR-181a expression in LC and EC were comparable. The most intensive staining was miR-17 in placenta in EPE, than the other groups of study ($p > 0.05$). MiR-210 was evaluated predominantly in mesenchymal stroma cells in EPE, but in LPE was higher in syncytium and syncytial knots.
Conclusion: Thus, impaired synthesis of miRs by placental structures (including miR regulating trophoblast proliferative activity), leads to preeclampsia.

PS-17-009
High frequency of viral genomes in paediatric chronic lower respiratory disorders: Nasopharyngeal aspirate as a valid substrate to detect viruses
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Objective: Chronic/recurrent lower respiratory disorders (C/RLRDs) include different diseases etiologically difficult to recognize and problematic to treat. The diagnostic value of nasopharyngeal aspirate (NPA) for the screening of respiratory viruses in C/RLRDs is poorly studied.
Method: We investigated respiratory viruses in NPA and bronchoalveolar lavage (BAL) from 133 children with different forms of C/RLRDs by polymerase chain reaction to investigate sensitivity, specificity and predictive values of NPA compared with BAL. 7 patients with persistence of symptoms repeated NPA after a mean follow-up of 6.4 months.
Results: At least one viral genome was detected in 60 % of NPA, often in combination: amplified viral sequences included particularly rhinovirus (HRV) (59 %), Epstein-Barr virus (31 %), herpesvirus 6 (29 %) and adenovirus (18 %). Sensitivity and specificity of NPA were high in detecting the most frequent viral genomes in C/RLRDs; multi-alignment and phylogenetic analysis showed a high identity among HRV sequences obtained from BAL and NPA of the same patient, but low identity with HRV sequence detected in NPA sample obtained 4 months later.
Conclusion: NPA is a less invasive tool with adequate sensitivity and specificity in the detection of viral genomes implicated in CLRDs. The detection of the same virus with different type species in the follow-up could be related to a high susceptibility to viral infections of these patients.

PS-17-010
Neuromuscular hamartoma/choristoma of the sciatic nerve with unilateral limp hypoplasia
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Objective: Neuromuscular hamartomas (NMH) are a rare cause for a unilateral atrophic limp with muscle atrophy and pain. NMH is a benign peripheral nerve lesion. We report a case of an 8-year old girl who presented with a hypoplastic left leg. Imaging studies suspected a plexiform growing PNST (perineurinoma, plexiform neurofibroma).
Method: The nerve lesion was sampled and the white-reddish specimen was submitted for histological examination. H + E stains and multiple immunohistochemical stains were performed.
Results: The biopsy revealed a multinodular lesion separated by thin fibrous septae. The lesion was composed predominantly of large pale

eosinophilic cells with a faint pattern of striation. These large cells expressed desmin, myogenin and MyoD1. The adjacent smaller spindled cells expressed S100 and represented the admixed nerve fibres. These features were consistent with a neuromucsular hamartoma/choristoma(NMH).
Conclusion: Usually, NMHs occur in cranial and large peripheral nerves. 9 cases are reported in the literature of which 7 patients are children (1–11 years) and 3 patients are adults (18–68 years). NMHs are slowly growing tumours. The clinical picture of limp deformity, muscular atrophy and pain will progress. The treatment options are limited and the outcome depends on the size and the location of the tumour.

PS-17-011
The possibilities of postmortem MRI for the differential diagnosis of stillborn and death of newborn
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Objective: To explore the possibilities of postmortem MRI for determining the stillbirth and spontaneous breathing of the newborn who died in the first day after birth.
Method: Investigated the bodies of 19 antenatal died stillbirths at gestational period 22–39 weeks, and 10 newborns who died after 2 hrs–5 days after birth. Postmortem MRI conducted before the autopsy. On T2WI in the sagittal projection was measured MR-signal intensity (SI) in the lung tissue (L) and shoulder muscle (M). Calculated the breathing index (BI) by the formula: SIL*SIM/100. During the autopsy evaluated pulmonary swimming test, macro- and microscopic examinations. 7 newborns without lung pathology constituted the control group for MRI.
Results: The values of BI were compared with the results of the autopsy. Positive pulmonary test was in all dead newborns, negative - in stillbirths. The BI average value in stillbirths (2185.4 ± 269.8) (values ranged from 756 to 3744) is significantly higher than the average BI in the dead newborns (481.8 ± 46.3, $p < 0.05$) (305–696). The BI average value was 91.7 ± 35,2 (values ranged from 53 to 154) in the control group. 700 - boundary BI-value for the differential diagnosis.
Conclusion: Using postmortem MRI allows to differentiate death newborn, which breathed and intrauterine fetal death.

PS-17-012
Familiar occurrence of desmosis of the colon: Report of two cases and literature review
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Objective: Gastrointestinal motility disorders are relatively common in children and adolescents. The diagnosis is often difficult and time-consuming as the etiology of the problems includes different pathological entities.
Method: Two adolescent girls who were familiar related (the same mother, different fathers) and both of them suffered from chronic constipation. Microscopic evaluation of full-thickness intestinal biopsy as well as post-operative material from total colectomy were analyzed in both cases. Following histological stains were performed: routine H&E and picrosirius red.
Results: In both cases normal ganglion cells were present in biopsy and post-operative material. Staining with picrosirius red revealed complete lack of the mesh network of collagen in the intestinal wall supporting the diagnosis of desmosis of the colon.
Conclusion: Desmosis of the colon is a very rare disorder causing constipation and its familiar occurence may suggest genetic background of the disease. Further studies on the subject with larger groups of patient, both paediatric and adults, are needed.

PS-17-013
A case of intrauterine Epstein-Barr virus infection
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Objective: Epstein-Barr virus (EBV) a ubiquitous gammaherpesvirus prevalent in 90 to 95 % of the human population. In spite of the fact that a large proportion of women at childbearing age are seropositive to this virus primary or secondary infections with this virus may occur during pregnancy. Primary infection with EBV during pregnancy with apparent transplacental transmission is rare.
Method: We report of the case of vertical EBV infection with damage of lungs and encephalitis. This is a case of an infant girl born at 29 weeks gestational age. EBV-specific immunostains (Novocastra) were studied.
Results: Birth weight was 1500 g. The lungs histology the presence of respiratory distress syndrome and viral pneumonia with lymphocytic invasion. In brain was showed lymphohistocytic inflammation and focal necrosis. The placenta's weight was 300 g. Macroscopic placental examination shows slight and unspecific changes. Histology demonstrated chronic villitis with lymphocytic invasion. EBV-specific immunostains with brain, lung, and placenta were studied and were positive.
Conclusion: Thus, in our case we IHC verified intrauterine EBV infection.

PS-17-015
Evaluation of relationship between chorangiomas and hypoxia-related placental changes in singleton and multiple pregnancy
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Objective: The aim of our study is to evaluate hypoxia-related morphological characteristics in singleton and multiple placentas which have chorangioma.
Method: Chorangioma was detected in 13 of 720 placentas examined at Pathology Department of Baskent University between 2011 and 2016. Histopathological findings of chorangiomas (tumour diameter, localisation, number of lesion, structural features) and hypoxia-related changes (villous maturation, infarct, vessel changes) were evaluated retrospectively.
Results: Six of 13 chorangiomas were detected in multipl pregnancy. The average of gestational age of placentas was 34,8 weeks in singleton placentas and was 34,6 weeks in multiple placentas. The average diameter of chorangioma was 1,4 cm in singleton placentas and 0,6 cm in multiple placentas. There were no significant differences in gestational age and average diameter between singleton and multiple placenta groups, respectively (p = 0,94/0,77). Majority of tumours were in subchorionic localisation (77 %) and have noduler structure (46 %). In the evaluation of hypoxia-related changes, distal villous hypoplasia was detected in 53 % of chorangiomas. The frequency of infarct was in 61 % and smooth muscle persistans was in 23 %. There were no desidual arteriopathy findings.
Conclusion: The findings suggest that there is a strong relationship between chorangioma and hypoxia

PS-17-016
Cystic malformation of the pulmonary airway: Report of 12 cases
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Objective: Cystic Malformation of the Pulmonary Airway (CMPA) is a generally benign alteration, manifesting commonly between 0 and 2 years

of life. The cysts vary between 0.3 and 6 cm, being predominantly multiple. The modern classification is: type 1-large cyst , 2- small cyst and absent cysts in macroscopy . This study was designed for analyse incidence of CMPA in a Children's Hospital of Fortaleza.
Method: A retrospective cross-section study was conducted reviewing slides of CMPA between 2008 and 2015.
Results: Twelve cases were analyzed with age group : 1 newborn, 7 infants, 2 preschoolers and 2 school children with 50 % girls and 50 % boys. Invariably they presented with dyspnea, reduction of vesicular murmurs and radiological alterations.Pathologic analysis based on new classification revealed 11 cases type 1 and 1, type 2.None of the cases had evidence of bronchial atresia (BA). The imaging tests more used were ultrasound and computer tomography and the surgery performed was lobectomy.
Conclusion: This evaluation shows that the most commonly found subtype is type 1.The present study highlights the absence of frequent BA associated and more slides of each case maybe needed to evaluate BA.

PS-17-017
A rare entity: Congenital cystic adenomatoid malformation in association with pleuropulmonary blastoma
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Objective: Presenting this rare case with the concurrent diagnosis of congenital cystic adenomatoid malformation (CCAM) type IV and pleuropulmonary blastoma (PPB) type I, we seek to improve the controversial relations between the diagnosis and management of these disorders.
Method: The patient was a 2 years old male toddler who was brought to hospital with the complaint of coughing and recurrent upper respiratory tract infections. A cystic mass lesion was found in patient's superior segment in the left lower lobe of lung as observed in computerized tomography scanning. Superior segmentectomy of the left lower lobe of lung was carried out.
Results: The specimen was macroscopically maroon-brown colored, 11x6x2 cm in size, and ruptured-cystic in appearance. All of the specimen was sampled. Microscopically, almost the whole lesion showed cystic structures lined by flattened epithelium.Skeletal muscles, mucous cells, cartilage and non-lesion lung parenchyma were all absent. In only a small area, there was a cambium-layer like small primitive malign cells with some rabdomyoplastic differentiation. Immunohistochemical evaluation showed that epithelial cells were positive for TTF-1 and CK7, while small cells were positive for Desmin.
Conclusion: Inferring from these, we diagnosed the patient with PPB type I and CCAM type IV. Even though it is crucial to distinguish PPB since it may determine the management of treatment, it may be difficult to make a distinction between these two disorders. It is advised to evaluate the whole specimen throughly to find focus with primitive malign cells

PS-17-018
Childhood lymphomas in Jos, North Central Nigeria
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Objective: To document the morphologic and molecular attributes of lymhpomas seen in childhood at the Jos University Teaching Hospital[JUTH].
Method: A descriptive, retrospective study of archival records, paraffin blocks and glass slides of lymphomas seen in children at JUTH between 2008 and 2012. Using a limited panel of monoclonal antibodies,[LCA, CD20, CD3, and CD30] lymphomas were immunophenotyped. Distribution according to sex, site, morphology and cell lineage was represented using tables and pie charts.
Results: Childhood lymphomas constituted 17.9 % of lymphomas seen. Non-Hodgkin lymphoma[NHL] formed 85.7 % of cases, Hodgkin lymphomas,14.3 %. Burkitt and Diffuse large cell lymphomas constituted 64.3 % of NHLs, with Burkitt accounting for 35.7 %. The male to female ratio of 3:4. Frequency of nodal and extra-nodal lymphomas was equal while the age range was 2 to 15 years. 10 of the 12 NHLs were of B cell immunophenotype.
Conclusion: The predominance of high grade lymphomas replicates findings in other studies. There's a decreased Burkitt lymphoma burden,as compared to previous studies.This reflects a reduction in the prevalence of HIV and Plasmodium infections. Improved infection control, cancer awareness and screening modalities, can lead to sustained reductions in the occurrence of lymphomas.

PS-17-019
Placental mesenchymal dysplasia with 13q12.11 deletion in a female neonate
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Objective: Placental mesenchymal dysplasia (PMD) has been associated with Beckwith-Wiedemann syndrome, paternal uniparental disomy 6, trisomies, and Klinefelter syndrome. Androgenetic-biparental mosaicism is the most common molecular alteration seen in PMD.
Method: We present a case of a 25 week gestational age pregnancy with severely growth restricted fetus with absent end diastolic blood flow in umbilical and middle cerebral arteries, pericardial effusion, oligohydramnios, and thick placenta with 2-vessel umbilical cord, clinically suspicious for partial hydatidiform mole. On amniocentesis, the fetus showed the 46,XX karyotype with 13q12.11 deletion involving the GJB6 gene by microarray. The mother tested positive for opioids and marijuana. The 380 gm neonate died 20 min after delivery triggered by premature rupture of membranes.
Results: The 218.8 gm placenta was thick (4.7 cm) with wide pale striae running perpendicularly from the chorionic plate toward the maternal floor. Histologically, giant stem villi with thick dysplastic vessels, stromal myxoid change, and cistern formation were seen. p57 immunohistochemistry highlighted the cytotrophoblasts and villous stromal cells. The uterine pattern of chronic hypoxic placental injury, acute chorioamnionitis, and focal low grade fetal malperfusion were present.
Conclusion: This study adds the 13q12.11 deletion to known associations of PMD. Placental overlap lesions, may result in perinatal mortality associated with PMD.

PS-17-020
Placental pathology as a cause of stillbirth
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Objective: Comparative analysis of the frequency of the presence of placental pathology at stillbirth in 2010 and 2015.
Method: Analyzed statistical data of Rosstat on the causes of stillbirth in the Russian Federation in 2010 and 2015.
Results: Reducing the lower limit of the frequency of newborns registration from 28 weeks of gestation (in2010) to 22 weeks (in 2015) resulted to increase of the number of stillbirths from 8,300 to 11,453 and a stillbirth rate from 4.62‰ to 5.87. The placental pathology, which determined the death, was revealed at 45.1 % and 48.7 % in 2010 and 2015, respectively. In 2010, placental pathology most often identified in cases of death from intrapartum (51.2 %) and antenatal (49.4 %) hypoxia, bacterial sepsis

(50 %). In 2015, placental pathology prevailed in cases of death from intrauterine infection (66.7 %), intrapartum (51.4 %) and antenatal (51.2 %) hypoxia, pneumonia (51.2 %). Placental insufficiency and placental transfusion syndrome predominated among placental pathologies.
Conclusion: Placental pathology leads to the development of complications in the fetus and its death. Investigating it in cases of stillbirth contributes to the elucidation of thanatogenesis. Changing the lower bound when registering of stillborns is accompanied by a change in the number of stillbirths and the detection rate of placental pathology, contributing to fetal death.

PS-17-021
The detection rate of histological placental changes at preeclampsia
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Objective: To determine the detection rate of histological placental changes at preeclampsia.
Method: Studied 114 placenta: from 26 patients with early preeclampsia (before 34 weeks of pregnancy) of moderate (12) and severe (14) severity, 84 with late preeclampsia (after 34 weeks of pregnancy) moderate (62) and severe (22), 40 - with physiological pregnancy (12-early and 28-late control). The analysis of the frequency of detection and diagnostic significance of the number of syncytial knots in the villi (SK), cell islands of extravillous trophoblast (CI) and microcysts in the septa (MC) of the placenta.
Results: A moderate amount of SK in villi were found in 66.7 % of cases with early moderate and 64.3 % with severe preeclampsia. CI were observed in all cases of early preeclampsia of moderate severity and in 57.1 % of cases with severe. At late preeclampsia, CI were found in 67.7.7 and in 68.2 % with moderate and severe, respectively. At moderate and severe early preeclampsia, MC was determined in 66.7 and 64.3 % of observations, respectively. For late preeclampsia MC were found at 56.5 % with moderate and 68,2 %—in severe.
Conclusion: The detection rate of histological placental changes of the placenta depends on the type (early vs late) and severity (moderate vs severe) of preeclampsia.

PS-17-022
Frequency of detection and localisation of air accumulations in the bodies of stillborn does not depend on the degree of maceration: Computed tomography and pathological comparisons
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Objective: To study the localisation characteristics of air accumulations in organs and tissues of stillborn by using postmortem CT.
Method: It was investigated the 21 bodies of the stillborn, who antenatal died on gestational age 22–39 weeks. Before the autopsy, conducted postmortem CT. Determined the localisations of air accumulations on the tomograms. During the autopsy, evaluated the degree of maceration.
Results: Time of intrauterine death ranged from 4 hrs to 2 weeks. When KT, air accumulations observed at 38.1 % of cases, their severity did not depend on the prescription of intrauterine death and degree of maceration. Air was visualised in the liver vessels at 87.5 %. Air in the cavities and vessels of the heart, as well as in mesenteric and cerebral vessels was observed at 62.5 %. Air was not visualised in the lungs, in the lumen of the stomach and intestines.
Conclusion: Localisation and frequency of detection of air accumulation in the bodies of stillborn did not depend on the degree of maceration. Most often, the air accumulation visualised in the cases where the residence time of the fetus in the uterus after his death was from 1 to 3 days. Air most frequently (87.5 %) was localised in the blood vessels of the liver.

PS-17-023
Maternal, fetal and placental factors associated with chronic villitis
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Objective: The objective of this study was to evaluate the relationship between fetal, maternal, placental factors and chronic villitis (CVUE) of unknown etiology.
Method: We analyzed 153 placentas from the archives of the Department of Pathology at Baskent University during an one-year period. Placental pathology reports and medical records were reviewed .The study involved specimens from two groups of i) CVUE group, 27 cases with CVUE (mean age, 32 years, range 19–42 years) and ii) control group, placental specimens of histopathologically normal from 36 cases (mean age,30 years, range 20–40 years). Maternal and fetal demographic data, risk factors and associated placental pathologies were assessed and correlations were analyzed in each study group.
Results: Among the maternal factors, the smoking rate was significantly higher in CVUE group compared with control group. Smokers were 14 times more likely to have chronic villi than non-smokers .In terms of fetal factors, jaundice, intra-uterine growth restriction , hearing loss, oligohydramnios and low birth weight rates were higher in CVUE group. There was no significant relationship between the severity and extent of inflammation and fetal and maternal factors.
Conclusion: The findings suggest that smoking plays an important role in the development of CVUE. Besides, CVUE causes several pathologies in fetus

PS-17-026
What is more with congenital lung abnormalities?: Multicentric perinatal and fetal autopsy review
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Objective: Congenital lung abnormalities are being detected more frequently at routine high-resolution prenatal ultrasonography. The most commonly encountered anomalies include lung agenesis-hypoplasia complex (pulmonary underdevelopment), congenital pulmonary airway malformations (CPAM), lobulation and position abnormalities, congenital lobar emphysema (CLE), Congenital Pulmonary Lymphenjiectasia (CPL) and bronchopulmonary sequestration.
Method: In this study we reviewed all fetal and perinatal authopsy cases of two centers in Antalya and we evaluated the cases with congenital lung disorder and their associated anomalies.
Results: Among 1095 autopsy cases 107 cases (9.7 %) had congenital lung disorder. Most common disorder was pulmonary hypoplasia with a percentage of 48.6 % (52 cases) and followed by immaturity (17 cases, 15.9 %), lobulation and position abnormalities (10 cases, 9.3 %), CPAM (8 cases, 7.5 %), vascular hypertrophy (8 cases, 7.5 %), CLE (4 cases, 3.7 %), agenesis (3 cases, 2.8 %), CPL (2 cases, 1.9 %), sequestration (2 cases, 1.9 %) and bronchopulmonary dysplasia (1 case, 0.9 %). Among 107 cases 62 cases (57.9 %) were associated at least one other congenital abnormality.
Conclusion: One of the most important point is associated anomalies. Recognizing the antenatal and postnatal imaging features of these

abnormalities and exhibit the associated anomalies is necessary for optimal prenatal counseling and appropriate peri- and postnatal management.

PS-17-027

Comprehensive detection of CFTR variants using anchored multiplex PCR and next-generation sequencing

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Objective: Cystic Fibrosis (CF) is an autosomal recessive disease caused by mutations in the CFTR gene. Carrier identification and newborn screening have significant implications in the overall prognosis of CF patients. However, current CFTR genotyping assays fail to detect mutations that are prevalent in non-white ethnic groups and cannot detect large deletions, which commonly drive CF pathogenesis in certain European populations. We present a method based on Anchored Multiplex PCR (AMP™) and NGS for comprehensive, pan-ethnic detection of CFTR variants, including large deletions.
Method: AMP uses unidirectional gene-specific primers and molecular barcoded adapters for amplification of known and unknown mutations. Anchored primers amplify large genomic regions from both ends independently, permitting independent sequencing of both wildtype and variant alleles.
Results: We show 100 % accuracy of CFTR variant detection, and identified 34 unique mutations in a blinded screen of 1,585 U.S. clinical samples. This revealed ethnic-specific CFTR variants, 73 % of which are not included in current ACMG guidelines for CF carrier screening. Furthermore, we detected the severe CFTRdele2,3(21 kb) in a prevalidated DNA sample.
Conclusion: We demonstrate that AMP-based NGS enables comprehensive detection of both known and novel variants in the CFTR gene, with the ability to detect large deletions.

PS-17-028

Gorham disease: Multifocal lesions in a child

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Objective: We describe an unusual case of Gorham disease with multiple involvement lesions in a child.
Method: Microscopic examination and immunohistochemical study were perfromed.
Results: A 3-year-old boy had a 20 month history of spine deformity with no history of trauma, or surgery. Physical examination showed a thoracic scoliosis without gait disorders. Standard blood laboratory tests were normal. Thoraco-abdoWe describe an unusual case of Gorham disease with multiple involvement lesions in a child.minal CT scan showed spine extensive osteolysis associated with a large non enhancing soft tissue mass in the posterior mediastinum. Bone involvement also concerned scapulae, ribs and pelvic girdle with soft tissue extension in the pelvic region. Surgical biopsy in the left girdle region was performed. The microscopic examination showed vascular proliferation with anastomotic thin walled lymphatic vessels between the remaining bony trabeculae. Immunohistochemical analysis disclosed that endothelial cells were positive to D2-40 antibody.
Conclusion: Gorham disease is a rare disease. Its exact etiology is still unknown. It is considered to be due to nonmalignant, neoplastic proliferation of hemangiomatous or lymphangiomatous tissue. Unifocal involvement is usual, while multifocal involvement such as in our case is rarely observed. Imagery reveals foci of intramedullary and subcortical lucency resembling patchy osteoporosis and enables biopsy guidance. Differential diagnoses include osteomyelitis, metastasis, osteolysis secondary to rheumatoid arthritis and hyperparathyroidism. The medical treatment for Gorham's disease includes radiation therapy, anti-osteoclastic medication and alpha-2b interferon. Prognosis for patients is generally good unless vital structures are involved.

PS-17-029

Atypical cloacal dysgenesis sequence: A case report

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Objective: The cloacal dysgenesis sequence (CDS) is a lethal complex congenital malformation. It results from a failure of division of the cloaca by urorectal septum to form the urogenital sinus and anorectal canal at a very early stage of embryonic development.
Method: We report a case of CDS associated with Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) and gonadal dysgenesis in a female newborn of 34 weeks of gestation. She was delivered by caesarean section for fetal distress, but she died shortly after birth. The karyotype was normal.
Results: The fetopathological examination confirmed multiple malformations including ambiguous genitalia, esophageal atresia with tracheœsophageal fistula, bilateral ureteropyelohydronephrosis, megacystis, urethral agenesis, colo-vesical fistula, permeable ouracus and single umbilical artery. Two gonadal strips, measuring 7 and 17 mm along their major axis, have been identified on both sides of a septated cystic mass without identifiable female genital tract. Histological examination showed a dysgenetic ovary and an undifferentiated contralateral gonadal tissue. At the vesical level, the wall of the upper cavity draining the ureters was of histologic bladder structure, while that of the lower blind cavity was of vaginal structure.
Conclusion: The association of MRKH syndrome and gonadal dysgenesis has been described in the literature and could be linked to a mutation or deletion of genes involved in the development of müllerian derivatives and gonads. To our knowledge, this is the first report describing an association of these genital abnormalities with cloacal dysgenesis.

PS-17-030

Small cell undifferentiated hepatoblastoma: A misnomer representing malignant rhabdoid tumour

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Objective: Malignant rhabdoid tumours (MRT) of liver are rare aggressive paediatric liver tumours. The molecular hallmark of these tumours is presence of deletions and/or mutations of SMARCB1 or rarely SMARCA4 leading to absence of INI1 or BRG1 proteins. The histologic diagnosis is based on INI1 negative immunoreactivity and presence of rhabdoid morphology. MRT lacking classic rhabdoid morphology are often misclassified as small cell undifferentiated hepatoblastomas (SCU-HB), according to the current Children's Oncology Group classifications.
Method: Five cases of INI1-negative paediatric liver tumours were identified from the Columbia University Department of Pathology Archives. In addition, immunostains for pancytokeratin, hepatocellular markers (Heppar, Arginase), and glypican-3, as well as Columbia Combined Cancer Panel (CCCP) were performed on formalin-fixed tissue.

Results: All tumours showed absence of hepatocellular markers and loss INI1/BAF47 staining. Glypican-3 staining was variable, and all except one showed positivity with pancytokeratin stain. Initially only two cases were diagnosed as MRT (focal rhabdoid histology). CCCP showed deletion of SMARCB1 in four cases and mutation of SMARCA4 in one case, confirming the diagnosis of MRT in all cases.
Conclusion: Morphology is unreliable for diagnosis of MRT. It is critical to classify INI-negative SCU-HB as MRT, and to eliminate the term INI-negative hepatoblastoma from the current classification scheme.

PS-17-032
Type II congenital pulmonary airway malformation involving entire lung - second trimester presentation with early demise
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Objective: We present a rare case of Congenital pulmonary airway malformation, Stocker Type II, causing severe intrauterine distress and early demise at 27 weeks of gestation.
Method: A 27 week-old baby was delivered by emergency Caesarean section to a 30 year-old G4P1 lady following absent foetal movements and rapid CTG decelerations. The lady had two previous first trimester miscarriages and a normal term pregnancy. The Ultrasound prior to surgery suggested left lung CPAM. The baby passed away a few minutes after delivery.
Results: Post mortem examination showed a large 172gram left lung, displacing the heart and a hypoplastic right lung. This lung mass had normal pulmonary vascular connections and no evidence of a separate systemic vascular supply. The cut surface of this mass was predominantly solid with a few subpleural small cystic spaces. There was no evidence of extrapulmonary anomalies. There were ambiguous external genitalia but female genital organs were identified intrabdominally. Histopathological examination of the lung mass showed innumerable cysts of small diameter (largest epithelial-lined cyst was 1.3 mm), lined by bronchiolar epithelium (cuboidal to columnar), and separated by thin alveolar septae, which in most areas included thin wisps of bronchiolar smooth muscle. The findings were those of Type II Congenital pulmonary malformation, which accounts for approximately 15 % of CPAM cases.
Conclusion: CPAM presenting in the second trimester is rare, and the poor prognosis in this case was directly related to the mass displacement created by the lesion, whereas usually the prognosis of Type II CPAM is related to extrapulmonary anomalies.

PS-17-033
Majewski syndrome: Histological features of kidneys, liver and lungs
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Objective: Majewski syndrome (MS), also known as short rib polydactyly syndrome type 2, is a rare autosomal recessive lethal osteochondrodysplasia characterized by short ribs, poly-syndactyly and micromelia with characteristic short ovoid tibiae. Visceral involvement is usually reported.
Method: We reported a case of MS in a full-term male neonate, that was diagnosed by antenatal ultrasound at 20 weeks of gestation, but the parents did'nt opt for termination of the pregnancy. The diagnosis was subsequently confirmed by postnatal radiography, autopsy and histopathology.
Results: The newborn showed characteristic craniofacial dysmorphism, short and narrow chest, micromelia, postaxial polydactyly, polysyndactyly and ambiguous genitalia. Postnatal X-ray showed short ribs, short long tubular bones with rounded metaphyseal ends and short ovoid tibiae. Autopsy revealed hypoplastic lungs, bilateral enlarged multicystic kidneys, cirrhotic hepatomegaly, left polycystic epididymis, cardiac hypertrophy and accessary spleen. Histological examination showed characteristic corticomedullary cysts of both kidneys, portal fibroadenomatosis and cystic dilatation of the airways.
Conclusion: This case report emphasizes the broad phenotypic spectrum of MS. The fetopathological examination is important to distinguish this condition from other disorders with micromelia, thoracic dysplasia and polydactyly, and to give adequate genetic counseling.

PS-17-034
Neonatal hemochromatosis: Report of an autopsy case
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Objective: Neonatal hemochromatosis (NH) is a congenital lethal alloimmune disease. It is characterized by hepatic and extrahepatic siderosis sparing the reticuloendothelial system. The most important pathological features are heavy liver siderosis and siderotic cirrhosis resulting in hepatic failure at birth.
Method: We described a case of NH complicated with hydrops fetalis and fetal death due to iron overload and severe liver disease.
Results: The 37-week-old male stillborn was born to a 37-year-old woman with history of gestational diabetes and miscarriage. The antenatal ultrasound performed before fetal death showed severe fetal hydrops and heterogenous hepatic structure. On postmortem examination, the fetus had facial dysmorphism, cardiomegaly with marked ventricular hypertrophy, splenomegaly and cirrhotic hepatomegaly. Microscopically, the liver architecture was distorted with extensive portal bridging fibrosis and marked siderosis of hepatocytes. Hemosiderin deposits were also demonstrated to a lesser extent in renal tubules, pancreatic acini and zona glomerulosa of the adrenal cortex. Reticuloendothelial siderosis was absent. Fibrous thickening of the splenic tissue was noted.
Conclusion: This case supports the importance of the autopsy in establishing the diagnosis of NH which is associated with high risk of recurrence. Thus, genetic counseling and prevention of recurrence in subsequent offspring using intravenous immunoglobulin can be provided to the family.

PS-17-035
Immunohistochemical study and prognostic value of Corin protein in preeclamptic placentas
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Objective: Preeclampsia constitutes an embryonic disorder characterized by aberrant functioning of the vascular intima and vasospasm. Clinically, it can be diagnosed through hypertension and proteinuria, resulting in abnormal placentation. Transmembrane serine protease, Corin, transforms pro-ANP to active ANP, which regulates blood pressure. In this regulation, also, contributes the process of the proteolytic cleavage. The purpose consists of the immunohistochemical study of Corin expression and its correlation to tissues' histopathology.
Method: Fifty placental specimens, either normal or preeclamptic, were obtained and then processed histologically. At the next step, they were immunohistochemically analyzed in order to evaluate Corin's expression.
Results: After observing all the processed tissue samples, we detected decreased expression of Corin protein on the pathological placentas in comparison with non-preeclamptic ones. More notably, the aggregation of the preeclamptic specimens displayed hypoexpression of Corin

protease. However, the normal placental tissues demonstrated higher Corin expression.
Conclusion: According to our results, Corin hypoexpression inextricably correlates with the appearance of preeclampsia. Thus, Corin could be considered as a remarkable prognostic biomarker in fetal tissues as far as preeclampsia is concerned. Nevertheless, there are relatively few investigations concerning Corin's expression in preeclampsia, thus, its crucial role awaits further elucidation.

PS-17-036
Placental terminal villi adaptations under maternal congenital heart disease conditions
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Objective: Placental villi structural adaptations in cases of maternal congenital heart disease (MCHD) are the necessary condition for successful gestation. The aim of the study was to characterize the features of the terminal placental villi under MCHD conditions.
Method: 35 placentas were divided into groups: I - 20 cases of MCHD and 15 cases of uncomplicated pregnancy (control group). Terminal villi features were evaluated microscopically and by the computer morphometry. Differences between groups' data were evaluated with the help of non-parametric test of Wald-Wolfowitz. The following format of the description of data was used Me (QR), where Me - median; QR - the interquartile range. Reliability established at $p < 0.05$.
Results: Results have shown the decrease in the surface area (SA) and diameter (D) of the placental terminal villi at marginal, paracentral and central zones of placental disk. SA in cases of MCHD were 2519,52(311,18); 2712,54(219,07); 2748,96(125,63) mmk2 (correspondingly: 2999,06(141,98); 3224,11(295,70); 3225,02(220,74) in controls). D in the in the group I decreased to 56,63(3,50);58,77(2,38);59,16(1,35) mmk compared with control data: 61,54(1,56); 64,07(2,97);64,08(2,21)mmk.
Conclusion: Villous tree adaptations to circulatory hypoxia in cases of MCHD result in the terminal villi proliferation at central, paracentral and marginal zones of placental disk, which support the adequate maternal and fetoplacental metabolism.

PS-17-037
Fetal giant cutaneous hemangioma associated with axillary arteriovenous fistula and complicated with severe congestive heart failure
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Objective: Hemangiomas are benign vascular tumours that are usually small and involve the skin and subcutaneous tissues of the head and neck regions. Here, we reported a case of congenital cutaneous hemangioma of uncommon size and location.
Method: We described a giant cutaneous hemangioma involving the right arm of a hypotrophic 32-week-old male fetus, which was detected by the early third trimester ultrasound and complicated with severe hydrops fetalis. The pregnancy was interrupted and a complete autopsy was achieved after parental consent.
Results: On macroscopic examination, the hemangioma was confirmed as a 5x5 cm raised violaceous and ulcerated mass with well-defined borders. The surface's cut showed tumour extension into dermal and subcutaneous layers with characteristic spongious architecture. A right large axillary arteriovenous fistula was noted. The microscopic appearance was consistent with a mixed capillary cavernous hemangioma. The dermal and subcutaneous vascular channels were lined by mature CD31-positive endothelial cells.
Conclusion: Hemangioma is a benign vascular tumour that may justify interruption of the pregnancy because of its significant size and hemodynamic complications. The etiology of this condition remains unknown. But, the histological appearance support the theory that consider hemangioma as a non-neoplastic disease of angiogenesis, stimulated by growth factors.

PS-17-038
Ultrastructure features of syncytiotrophoblast and syncytial knots of placenta villi in cases of preeclampsia
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Objective: Syncytial knots (SK) were known to be syncytiotrophoblast (STB) proliferation zones of closely spaced hyperchromatic nuclei surrounded by a common cytoplasm. The SK amount was common adaptive mechanism in the hypoxia, including preeclampsia (PE), but ultrastructural features of them have not been studied. The aim of study was to analysis of ultrastructure features syncytiotrophoblast &syncytial knots of placenta in cases of preeclampsia.
Method: The groups of the study included placenta samples of 17 women of reproductive age, 26–39 gestation weeks after cesarean section (5 women with severe PE and 4 with moderate PE and 8 women with physiological pregnancy (Control group). We performed histological and electron microscopy examinations.
Results: By electron microscopy in placenta samples in severe PE there the STB apical layer was damaged, without microvilli on the surface, with multiple cytoplasm vacuoles were also revealed (the vacuole diameter were 6–10 fold larger than Control). Moreover, in severe PE we detected SK surrounding by fibrinoid deposits (FD), nuclei of SK were with karyopyknosis. Although, FD were considered to protect syncytiotrophoblast from maternal lymphocytes, preventing allograft-type response development. FD were located in intravillous space that thickening placental barrier.
Conclusion: Trophoblast and syncytial knots alteration leaded to impairment placental barrier and hypoxia increased.

PS-17-039
Traps in the diagnosis of parotid adenoid cystic carcinoma: A paediatric case
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Objective: The most common childish salivary gland tumour is pleomorphic adenoma (PA). Adenoid cystic carcinoma (ACC) is a rare malign tumour in children.
Method: A 13-year old boy applied with a tumour in the left parotid gland observed 2 months ago. Ultrasound showed a homogeneous 19x16 mm solid hypoechoic nodule with regular margins.
Results: Fine needle aspiration biopsy (FNAB) provided an inadequate sample. Magenta-red stained epithelial and myoepithelial cell groups without obvious atypia were observed with Diff-Quik staining and were reported as pleomorphic adenoma. The tumour was removed with enucleation. A cream-pink solid nodular tumour with soft consistency and round-like regular margins were seen in macroscopic evaluation. The tumour had an obvious capsule, and it touched the surgical margin in focal areas. Parenchymal area other than the tumour was scarce. Perineural invasion was solely detected in two small areas at the periphery. It was reported as "low grade adenoid cyctic carcinoma, trabecular pattern".

Conclusion: paediatric ACC is generally aggressive. It can disseminate adjacent tissues without complying with anatomical plan. The tumour may have a regular margin, and there may not be any physical examination finding other than tumour. Finally, magenta-red material obtained through FNAB may not be a PA.

PS-17-040

Giant squamoid cyst of pancreatic ducts in childhood: A case report

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Objective: Squamoid cyst of the pancreas is defined as a very rare benign cystic lesion of the pancreatic ducts that is lined by bland nonkeratinizing squamous epithelium.
Method: A 4-year-old boy patient was admitted to our pediatric surgery out-patient clinic with abdominal pain. MRI demonstrated a unilocular cystic lesion sized 20x17x12 cm and located posterior of the pancreas. A preliminary diagnosis of mesenteric cyst was made and total cystectomy was performed. Surgical exploration of the patient revealed giant cystic lesion adjacent to tail of the pancreas. This lesion was filled with a yellow-green colored cystic fluid.
Results: Histopathological examination revealed that the cyst had linings ranging from flat squamoid cells to transitional cells with non-keratinization. The cyst walls were composed of relatively thin fibrous issue. None of columnar or mucinous component, associated lymphoid or splenic tissue, ovarian type stroma, adnexal structures, fibrosis, and pancreatitis were identified. Immunohistochemically, squamous differentiation was demonstrated by strong diffuse expression of p63 and CK5/6. The final diagnosis was confirmed as squamoid cyst of the pancreas.
Conclusion: Squamoid cyst of the pancreas is a very rare entity but it is extremly rare with this size at this age. It should be considered in the differential diagnosis of pancreatic cystic lesions.

PS-17-041

Thanatophoric dysplasia type I (Maroteaux-Lamy-Robert-Syndrome), a multidisciplinary approach

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Objective: Thanatophoric dysplasia is a severe skeletal dysplasia, defined by the presence of point mutations within Fibroblast Growth Factor Receptor 3 (FGFR3) gene, with an incidence of 1:20000–1:50000 live born infants. The phenotype is characterised by the presence of complex skeletal, neurological and respiratory anomalies, associated with failure to thrive and poor prognosis. The aim of this paper is to emphasize the necessity of an early diagnosis of thanatophoric dysplasia.
Method: We report the case of a newborn girl, from a young mother, with no prenatal care. Gestational age was 41 weeks, birth weight 2130 g, Apgar score 2/6/8. In the neonatal unit, severe growth deficiency, facial dysmorphism, macrocephalic head, pear-shaped thorax and micromelia were noted, suggesting a genetic syndrome. The clinical presentation and imaging studies sustained the diagnosis of thanatophoric dysplasia type I. Postnatal evolution was marked by the aggravation of pulmonary dysfunction, followed by exitus at the age of 2 months.
Results: Although genetic testing for FGFR3 were not performed, the patient presented numerous clinical and paraclinical elements highly suggestive for thanatophoric dysplasia, also confirmed at the post-mortem examination.
Conclusion: Prenatal diagnosis of thanatophoric dysplasia is essential in order to offer genetic counseling to an affected family. The treatment requires a complex multidisciplinary approach.

PS-17-042

Placental membrane remodeling in pregnancies complicated with maternal congenital heart disease

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Objective: Maternal congenital heart disease (MCHD) may cause a fetal hypoxia, various perinatal complications. The aim of study was to evaluate a placental membrane (PM) remodeling in the central, paracentral and marginal zones of placentas from pregnancies with MCHD.
Method: Placentas from pregnancies complicated with MCHD were examined grossly. Histological slides were studied microscopically and with computer morphometry. All material was divided into groups: I - 20 cases of MCHD and 15 cases of uncomplicated pregnancy (control group). Differences between groups' data were evaluated with the help of non-parametric test of Wald-Wolfowitz.
Results: PM in cases of MCHD reduced to 2,71(0,08), 2,57(0,15), 2,39(0,23) mmk correspondingly in the central, paracentral and marginal zone of the placenta (controls - 3,58(0,16), 3,58(0,16), 3,51(0,17) mmk, $p < 0, 05$). Capillaries more often were located on the periphery of the terminal villi. Therefore, volume fraction of a vascular-syncytial membranes (VSM) increased to 18(10), 16(8), 16(8) % in the central, paracentral and marginal zone compared with controls (correspondingly - 12(8), 12(12), 12(8) %, $p < 0, 05$).
Conclusion: The thinning of placental barrier and increased length of a VSM contributes to the activation of the oxygen and nutrients supply via PM and supports intrauterine fetal development in cases of MCHD.

PS-17-044

Two rare cases of lipoblastoma; Inguinal region and mandibular corpus

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Objective: Lipoblastoma is a rare benign mesenchymal tumour composed of adipose tissue in early childhood and infants. Lipoblastoma is frequently seen in extremities, trunk, head and neck. We present two lipoblastoma cases:
Method: The first case was a 3-year-old female presented to our hospital with a palpable mass in right inguinal region. Tumour was resected tottally. Grossly, the tumour measured 8x4x4 cm in diamater. The second case was a 2-year-old female was admitted to our hospital with a painfull and palpable mass in the corpus of left mandibula. Incisional biopsy was performed. In pathological examination, the tumour was 2x1.7x1 cm in diamater grossly.
Results: Histologically in both cases, were composed of fatty lobules which were separated by fibrous septas, tumour had myxoid areas, and plexiform vascular pattern composed of adipocytes in various maturation stages. In immunohistochemical investigation of these two cases, lipoblasts showed positive staining with S-100 protein and Ki-67 proliferation index was %10, 2–3 %, respectively. The diagnosis was lipoblastoma.
Conclusion: Especially in children younger than 3 years, lipoblastoma diagnosis should be kept in mind when encountering a lipomatous mass. Lipoblastomas prognosis' is excellent, to prevent recurrensies wide local excision is advised.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-18 Autopsy Pathology

PS-18-001
Causes of death in patients with lung cancer
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Objective: To determine causes of death in patients with lung cancer.
Method: Retrospective study was performed on autopsy report data from 213 patients with lung cancer who died in Institute of lung diseases of Vojvodina in period from 1962 to 1975.
Results: During 14 years period 1483 autopsies were performed, 213 in patients with lung carcinoma. Mean age in deceased with lung cancer is 58,7 (range 24 to 85 years), predominantly males (83 %) over females (17 %). Types of lung cancer were reclassified as small cell carcinoma in 32 cases (15,1 %) and non-small cell carcinoma in 191 cases (84,9 %). Two patients had syncronous cancer (colorectal carcinoma and squamous cell carcinoma of epiglottis with non-small cell carcinoma of the lung). Most frequent causes of death in patients with lung cancer are infection (25,8 %), tumour burden including metastatic cancer disease (18,8 %) and pulmonary thromboembolism (17,8 %). Infection includes acute bronchopneumonia in 46 cases, tuberculosis and pleuritis in 3 cases each. The following causes of death are hemorrhage (13,1 %), cachexia (12,2 %), cardial causes (6,1 %) and other causes including aspiration of stomach content and bowel obstruction (3,7 %).
Conclusion: Patients with lung cancer are prone to infection and pulmonary embolism and it poses a challenge for prevention in the future.

PS-18-002
Validity of a minimally invasive autopsy tool for cause of death determination in paediatric deaths from Sub-Saharan Africa
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Objective: Our knowledge of what is killing children in low income countries remains poor, partly because of the inadequacy and reduced precision of the methods utilized.The minimally invasive autopsy (MIA) has been proposed as a substitute to the complete autopsy (CA) in poor settings. We assessed the validity of the MIA in determining the cause of death in 54 post-neonatal paediatric deaths in a hospital of Mozambique by comparing the results with those of the CA.
Method: Concordance between the categories of diseases obtained by the two methods was evaluated by the Kappa statistic and the sensitivity, specificity, positive and negative predictive values of the MIA diagnoses were calculated.
Results: A cause of death was identified in all cases in the CA and in 96.3 % of the cases in the MIA, with infections and malignant tumours accounting for the majority of diagnoses.The MIA showed a substantial concordance with the CA (Kappa = 0.70;p-value < 0.0001) and sensitivity, specificity and overall accuracy were high.The ICD-10 diagnoses were coincident in up to 75 %.The MIA allowed the identification of the pathogens in 78.1 % of infection-related deaths.
Conclusion: The MIA showed a substantial performance for cause of death identification in this series and could provide robust data for CoD surveillance in resource-limited settings.

PS-18-003
Analysis of postmortal diagnoses of patients died on the Institute for Pulmonary Diseases of Vojvodina during the 10 years period
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Objective: Analysis of sex and age of patient died at the Institute for Pulmonary Diseases of Vojvodina (IPDV) during a period of 10 years, as well as their primary disease, the cause of death, length of hospital days.
Method: We analyzed the autopsy records of all patients who underwent clinical autopsy in the period 2005–2015. The pathological diagnoses were grouped into 7 groups of diseases according to the International Classification of Diseases, 10th Edition. At the end Goldman's classification was used.
Results: It was autopsied total of 566 patients, average age 65.3 years, whereby 68.5 % were men. The most of the patients have died at the Urgent Pulmology Clinic (33 %), during the first 24 hrs of hospital admissions, in 37.8 % patients malignant primary disease was found and the most common cause of death was pneumonia (24.2 %). According to Goldman's classification the most of the analyzed autopsies showed full confirmation of clinical diagnosis- Class V (49.8 %), while Class IV was found in 9.2 %, Class III in 8.1 %, Class II in 17.1 % and Class I in 15.7 % of autopsied patients.
Conclusion: The autopsy is instrument for quality control, precise determination of the death cause, confirmation or correction premortal diagnosis and identification of new disease.

PS-18-004
An autopsy case of massive pulmonary tumour embolism due to undiagnosed prostatic adenocarcinoma
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Objective: To present a case of massive pulmonary tumour embolism due to undiagnosed prostatic adenocarcinoma.
Method: We report an autopsy case in which hematoxylin and eosin as well as immunohistochemical staining with prostate-specific antigen (PSA) showed multiple tumour emboli within small and medium sized pulmonary arteries.
Results: A 78-year-old man without remarkable medical history was admitted to our hospital with clinical symptoms suggestive of subacute pulmonary thromboembolism. He suffered from progressive dyspnea and general fatigue few days before admission and died after 5 hrs of hospitalization. Due to unknown cause of death autopsy was performed. On autopsy, enlargement of prostate was found and pathohistologically diagnosis of poorly differentiated adenocarcinoma with Gleason's score of nine was set. No metastasis in regional lymph nodes and bones were found. In all specimens taken from lungs multiple tumour emboli within small and medium sized pulmonary arteries were found. Tumour emboli were composed of atypical polygonal cells with slightly enlarged nuclei and prominent nucleoli which was arranged in small acinar and cribriform formations. Immunohistochemical analysis with PSA staining showed diffuse and strong positivity of tumour cells within pulmonary arteries.
Conclusion: A prostate adenocarcinoma can extremely rarely be a cause of massive pulmonary tumour embolism.

PS-18-005
Histopathological heart changes in autopsies of heroin abusers
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Objective: Heroin is a semisynthetic opioid that may cause morphological and histopathological changes in heart. The aim of the study is to show histopathological heart changes in autopsies of long-time heroin abusers with positive toxicological analysis for 6-monoacetylmorphine (6-MAM) and morphine in blood and urine.
Method: Retrospective study was done at the Institute of Pathology and Forensic Medicine Military Medical Academy in Belgrade between 2010 and 2014 and included forensic autopsies of 27 examinees aged between 18 and 60. Material of heart taken during autopsies was stained by hematoxyline-eosine (HE) and trichrome and microscopically examined.
Results: Myocardial fibrosis was found in 27/27(100 %) examined including perivascular fibrosis in 24/27 (88.89 %) and interstitial focal fibrosis in 3/27 (11.11 %). Hypertrophy of cardiomyocytes had 22/27 (81.48 %), myofibril contraction band necrosis 22/27(81.48 %), loss of myocytes nuclei and cross-striation 10/27(37.04 %), fresh perivascular bleeding 23/27(85.19 %) and focal inflammatory cells infiltrate 14/27 (51.85 %).
Conclusion: Our results indicate histopathological heart changes which are non-specific and could be caused either by long-term heroin abuse or by other factors. Having in mind lack of medical histories of examined we couldn't exclude other factors besides long-term heroin abuse as cause of heart changes.

PS-18-006
Time trends and causes of maternal mortality in Ceará State, Brazil from 2010 to 2014: Necropsy study and lessons from pathology
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Objective: To assess time trends in maternal mortality (MM) in Ceará, Brazil from 2010 to 2014, as to well to describe its main causes.
Method: Cross-sectional and retrospective study was carried out through the analysis of medical records and death certificates (DC) of necropsy cases obtained from the performed at the Death Verification Service (DVS), official state entity.
Results: During this period, there were 472 MMs in Ceará, 21.6 % were submitted to necropsy in DVS. The trend over the period was lowest in 2014 and highest in 2010 with diminution over period by −22.5 % per year. The immediates causes are Hypovolemic shock 20.5 % , respiratory failure 18.6 %, pulmonar edema and unspecified causes (CNS) both with 16.6 % . Among basic causes of death, 21.6 % was no record by professionals, mixed shock, hypertensive disorders of pregnancy and previous hypertension each with 10.8 %.
Conclusion: There was a decline in absolute number of MM during the period of study. Unfortunately, the MM rate is higher than that reported in the study, since the lack of information on the causes of deaths and the sub-registries of DCs make it difficult to officially record the data, thus contributing to masking knowledge about MM.

PS-18-007
Hirschsprung Disease Associated Entercolitis (HAEC): An autopsy case report
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Objective: HAEC is the greatest cause of morbidity and mortality among infants with Hirschsprung's disease (HD). HAEC may manifest as abdominal distension and explosive diarrhea along with emesis, and even shock.
Case report: A non-breastfed infant, born in term, was admitted to hospital 7 days after delivery with severe diarrhea and vomiting. Clinical examination did not reveal any cause of this condition and the infant was discharged, although the symptoms did not improve. Despite regular check-ups by a paediatrician, who recommended to change nutrition formula, symptoms progressed to lethargy. In spite of rapid transport to the Hospital the infant died at the age of 34 days due to septic shock. The autopsy revealed gross signs of pseudomembranous colitis.
Method: Histological examination of all segments of intestines was performed. Calretinin and GLUT-1 immunohistochemistry was carried out on paraffin-embeded tissues. Moreover, DNA for molecular genetic investigation was extracted from the skeletal muscle.
Results: Lack of ganglion cells along with negativity of calretinin and positivity of GLUT-1 in anorectal junction confirmed the diagnosis of HAEC. RET gene was found to be wild type.
Conclusion: Accurate and prompt diagnosis of HD is crucial and may prevent severe complications or even death.

PS-18-008
The importance of the fetal autopsy in the diagnosis of a novel mutation in SOX9 associated to campomelic dysplasia
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Objective: To characterise pathologically, radiologically and genetically a fetus of 13 weeks, for the consequent genetic counseling of the parents. The previous ultrasound diagnosis was an indeterminate polymalformative syndrome.
Method: Before the autopsy of the fetus was done, an X-ray examination was requested to identify possible osseous malformations. The pathological study was performed in a conventional way. DNA, previously obtained from placental chorionic villi, was used for the genetic study, and a wide panel of skeletal dysplasias was evaluated with Next Generation Sequencing.
Results: The findings in the radiological and pathological studies were: facial malformations, arthrogryposis, bilateral tibial spines, bowed limbs, narrowed thoracic spinal canal, among others which led to the diagnosis of Campomelic dysplasia. The massive sequencing showed a novel heterozygous mutation (SOX9:NM_000346.3:c.658_679del;p.Glu220Thrfs*26), confirming the diagnosis.
Conclusion: Campomelic dysplasia is a rare and severe disorder that affects the development of the skeleton, and other organs. Most cases are caused by mutations within the SOX9 gene. The findings from the autopsy were vital to conclude with the discovery of the new mutation in SOX9, not previously reported.

PS-18-009
Turnaround time of autopsy reports
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Objective: The turnaround time from autopsy to finished report is of major importance for clinicians, both for learning and for the follow-up of next of kin. As part of a larger project on the quality of autopsy reports, we have looked at the turnaround times in Norway.
Method: A survey about autopsy frequency and practise in 2015 was sent to all 15 departments of Pathology in Norway.
Results: In cases without fixation of the brain, turnaround times for the final reports were reported from the departments as more than 1-month in all but one department. Neuropathological examinations delayed the reports with up to several months. One department had turnaround times of 10 days without and 32 days with neuropathological examination. Short response times were due to widespread use of additional reports in cases

where special examinations of no importance for underlying death or for clinicians would result in delay of the final reports, as some neuropathological examinations. The same department also did not send preliminary autopsy reports, in contrast to the practise followed by all other departments.
Conclusion: Short turnaround times may be achieved by changing the way of reporting autopsy answers. The primary goal must be to ensure useful feedback to the clinicians before they forget or give up complaining.

PS-18-010
Case of politarteritis nodosa undiagnosed during life
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Objective: Systemic poliarteritis nodosa is a rare condition and diagnosis is often based on clinical manifestations. In absence of treatment, systemic poliarteritis nodosa is characterized by poor prognosis since the condition develops rapidly and is often fatal.
Method: Case of systemic poliarteritis nodosa which was not diagnosed during life was retrospectively analysed.
Results: The clinical manifestations of systemic poliarteritis nodosa appeared for very first time in a female patient (72 years old) after viral respiratory infection, and included dizziness, fatigue, and joint pain. Over the period of 5 months she was repeatedly admitted by different hospitals with diagnosis of 'encephalopathy', 'erosive gastritis', 'acute myocardial infarction'. In 10 days after latest discharge she was admitted to the hospital with massive gastrointestinal haemorrhage. In 6 days after latest admission the patient died. Despite obvious clinical manifestations of a systemic disease (including, fever, weight loss, encephalopathy), the final diagnosis was made only after a histological examination. Morphological manifestations of the disease included lesions of small and medium vessels in kidneys, gastrointestinal tract, myocardium, and lungs. Morphological changes were characterised by segmental fibrinoid necrosis or circumferential fibrinoid necrosis.
Conclusion: The patient was present with systemic poliarteritis nodosa, which became a cause of renal insufficiency and bowel infarction. The disease was characterised by gradual progression within the period of 5 months. Within this time period, the patient received symptomatic treatment in different hospitals, however, the correct diagnosis was never made, and therefore, administration of hormone therapy was impossible.

PS-18-011
Hidatidosis: A case report
R. Esteves*, A. da Costa Ferreira, M. H. Oliveira, A. Catarino
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Objective: We present an autopsy case of Hidatidosis seen in our department. Hydatidosis is a zoonotic disease caused by the Echinococcus parasite. Its different forms are a public health problem, which in Europe has its greatest expression in the Mediterranean basin. In Portugal it is a notifiable disease (2016 $n = 2$).
Method: Autopsy, cytology and histology
Results: Forty-one year-old man with a history of pulmonary and pericardial hydatid cyst surgically treated at age 21. He has an ICD. Two months earlier begins to suffer from haemoptysis and, in spite of the empirical antibiotic treatment, his condition gradually worsens. Chest CT scan and bronchofibroscopy were inconclusive. He goes into the emergency room in cardiorespiratory arrest, following massive haemoptysis refractory to resuscitation attempts. The autopsy revealed a bilateral multicystic pulmonary hydatid cyst with a fistula to a pulmonary artery branch and the presence of hydatids in the right ventricular cavity.
Conclusion: In high-prevalence countries, hydatidosis is an entity which clinicians should take into account in their differential diagnoses and which can be fatal if undiagnosed.

PS-18-012
A fatal case of idiopathic mesenteric venous thrombosis
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Objective: Idiopathic mesenteric vein thrombosis (MVT) is a rare type of intestinal ischemia associated with significant mortality and morbidity because of its diagnosis delay.
Method: A 32-year-old female patient was admitted to the Emergency Department complaining of right-lower abdominal pain. After physical examination and routine laboratory was done, laparascopy for suspected appendicitis was performed. The patient's condition was deteriorating and was transferred to Intensive Care Unit. CT-scan revealed a hypoattenuating venous filling defect with superior mesenteric vein enlargement. She was scheduled for second-look operation where small intestinal infarcted segment was resected. Unfortunately, the patient died 3 days after hospitalisation.
Results: Autopsy revealed superior mesentery vein thrombosis associated with small bowel infarction, fibrinopurulent peritonitis and disseminated intravascular coagulation. Analysis of genetic status for known prothrombotic mutations has revealed compound heterozygosity for 677C>T and 1298A>C in MTHFR gene and heterozygosity for Factor V R2 mutation. The assumed reduced MTHFR enzyme activity, combined with the genetic constitution, abdominal trauma and infection has lead to precipitation of thrombophilic disorders.
Conclusion: A screening of primary coagulation abnormalities must be carried out in all patients with MVT because they represent the most frequent cause of venous thrombosis. It would be rational to offer genetic testing for thrombophilia to at-risk family members before exposure to recognized risk factors.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-19 Cytopathology

PS-19-001
Role of cell block and immunocytochemistry in cytological diagnosis: A new dimension to diagnosis of cancer
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Objective: To analyze the role of cell block and immunochemistry(ICC) in fine needle aspiration cytology(FNAC) and malignant fluid cytology
Method: Retrospective descriptive analytical study done from January 2014 to February 2017 analyzing 8950 cases of FNAC and 8290 fluids. Cell blocks were prepared in 1920 cases. Immunocytochemistry(ICC) was done wherever required.
Results: Cell blocks with ICC helped in categorization of tumours in 224 FNAC samples. Commonest site was lymph node ($n = 102,45.5$ %) with diagnosis of metastasic carcinoma($n = 45,44.1$ %),metastatic melanoma($n = 03,2.9$ %),B-cell($n = 36,35.3$ %)and T-cell lymphomas($n = 18,8.17.6$ %). Pancreatobiliary lesions($n = 60,27$ %)-comprised high grade neuroendocrine tumours ($n = 28,46.7$ %),poorly differentiated adenocarcinomas($n = 18,30$ %),solid pseudopapillary neoplasms ($n = 08,13.3$ %) ,lymphomas($n = 03,5$ %),-metastasis($n = 02,3.3$ %%)and pancreatoblastoma ($n = 01,1.7$ %).Soft

tissue and subcutaneous lesions consisted of melanomas(n = 03)and metastatic carcinomas(n = 07).Gastrointestinal lesions included mesenchymal lesions like gist(n = 03),leiomyoma(n = 04)and metastasis(n = 02).Adrenal pheochromocytoma(n = 04) and adenoma(n = 02), small cell carcinoma(n = 08),and adenocarcinoma lung(n = 06) and liver metastasis were amongst other lesions diagnosed using ICC. In fluid samples,cell block with ICC helped to ascertain the primary site of malignancy in 38 and to prove metastasis in 115 cases.
Conclusion: Endoscopic Ultrasound and CT guided FNAC are used to sample deep seated and small lesions. In the era of personalized medicine, cell block with ICC is a useful tool for rapid accurate diagnosis which guides management decisions by helping in early initiation of therapy by obviating the need for a core biopsy.

PS-19-002
Fine needle aspiration cytology of the kidney correlated with histological data: A 17-year retrospective study
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Objective: Report our institution's experience with renal tumour fine needle aspiration(RTFNA) over a 17-years period, correlating with histology.
Method: RTFNA performed at our institution (2000–2017) were identified using SNOMED-based computer search. Demographic data, radiologic characteristics, cytological interpretation and histological diagnosis were recorded.
Results: 172 RTFNA cases (age(mean,range): 61(1–89)years; 114(66 %) male; lesion size:10–150 mm; radiologic characteristics: solid 106(61.6 %), cystic 32(18.6 %), mixed 19(11.6 %), not specified 15(8.7 %)). RTFNA diagnoses included neoplasm (76;44 %), "suspicious" (12;7 %), nonneoplastic (51;30 %) and unsatisfactory (33;19 %). Neoplastic diagnosis encompass renal cell carcinoma(RCC) (40), nephroblastoma(9), oncocytic neoplasm(6), metastasis(6), angiomyolipoma(4), lymphoma(2), carcinoma NOS(4) and other(5). Histology was available in 85(49.4 %) cases. In 10, the diagnosis was substantially different from RTFNA (RTFNA to histology): 6 "cystic contents" to RCC; 1 RCC to metastatic adenoid cystic carcinoma; 1 chromophobe RCC to atypical oncocytoma; and 2 likely sampling errors, "suspicious" to xanthogranulomatous pyelonephritis and "oncocytic lesion" to interstitial nephritis. RTFNA demonstrated 90.5 % sensivity and 66.7 % specificity for neoplastic lesions and 89.5 % sensivity and 58.3 % specificity for malignancy.
Conclusion: RTFNA has high sensitivity for the diagnosis of renal neoplasia and malignancy. In this series, specificity was mostly impaired by limitation in sampling and identification of neoplastic cells in cystic lesions. Nonetheless, RTFNA is a useful diagnostic tool for renal tumours.

PS-19-003
The accuracy of cytology in diagnosis of small cell lung cancer
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Objective: Small cell lung cancer (SCLC) is very aggressive, therefore early differentiation from other malignancies is important in influencing therapy. The aim of this study was to determine the accuracy of cytology in diagnosis of SCLC.
Method: One-year retrospective study done at the Institute of Pathology and Forensic Medicine, Military Medical Academy, Belgrade included 100 patients, 79 %(79/100) men and 31 %(31/100) women aged between 43 and 84(average 65.03 ± 8.36) with SCLC diagnosis. The value of cytology was determined by comparing May-Gruenwald-Giemsa stained smears with histological bronchoscopy samples. Data was statistically analysed using descriptive methods and Kendal-tau correlation (significance level $p < 0,05$).
Results: Most of cytological samples were obtained by trans-bronchial needle aspiration-73 %(73/100) and brushing biopsy-18 %(18/100). Among 100/100(100 %) cytologically diagnosed 93 %(93/100) were histologically confirmed. Histologically adenocarcinoma, non-small cell lung cancer and large-cell neuroendocrine carcinoma accounted each for 1 %(1/100), combined SCLC was found in 2 % (2/100). 2 % (2/100) were histologically benign. There is no statistically significant difference between cytological and histopathological diagnosis ($p = 0,202$). Sensitivity of cytology was 98.04 %, specificity 99.13 %, positive predictive value 93.46 % and negative 99.75 %.
Conclusion: Cytology is reliable method with good correlation with histology for diagnosing small cell lung cancer. In determining difficult cases it must be supported with immunostaining and additional methods.

PS-19-004
Continuing education for technicians in rapid on-site evaluation: Simulation pilot experience
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Objective: Rapid On-site Evaluation (ROSE) of the samples obtained using the Fine Needle Aspiration (FNA) cytology technique is considered crucial for appropriate management of patients who undergo such procedure. Traditionally, it is recommended that the pathologist or pathologist technician (cytotechnician) carry out this assessment. The utility of FNA simulators for this type of training was evaluated.
Method: FNA sessions were conducted in our center, in a simulated environment, using the puncture task simulators (ES1140059 and ES1149563), with loads of plant material (plantain pulp). The characteristics of this material, after being spread on slides and undergoing dyeing techniques (hematoxylin-eosin, Diff-Quick and Giemsa) make it suitable for a microscopic evaluation.
Results: A total of 20 FNA's were performed by one pathologist and 5 cytotechnicians, in a randomized and rotational manner, carrying out the processing of the material, its staining and microscopic visualization. In all cases, evaluable cellularity was observed and, therefore, was considered a sufficient sampling. The mean time from the start of the processing of the sample until its visualization under the microscope was 4′01″ (range 3′42″–4′26″).
Conclusion: - The task simulators are adaptable to scenarios to train cytotechnicians for in situ evaluation of samples obtained by FNA. - This allows the cytotechnicians to certify the quality of the sample obtained, optimizing resources and avoiding additional unnecessary procedures or FNA's. - The adequate training of cytotechnicians assures the patient a shorter time of exposure to the diagnostic procedure and its possible complications.

PS-19-005
Liquid-based techniques in urine cytopathology: BD SurePath® and Cytospin
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Objective: The purpose of this study was to show advantages of application of liquid-based technologies BD SurePath® and Cytospin in uropathology diagnostics.
Method: 110 specimens of voided urine sediment were investigated—33 from women, and 77 from men with different urinary tract diseases. All the samples were first centrifuged for 10 min, 2000 rpm, and then prepared using two techniques: Cytospin-3 (Thermo Scientific Shandon) in 5 min at

1500 rpm and BD SurePath®. Cytomorfology was evaluated according to the Paris System for Reporting Urine Cytology (2016).
Results: Using the method of ultimate cell concentration and the liquid-based technologies it was noted that analyzed samples contained up to 20 times more cells than traditional ones. In cases with histologically confirmed high grade urothelial carcinoma (HGUC) the sensitivity of cytological method was 57 % in conventional smears, 67 % in SurePath®, and 98 % in Cytospin-3 slides. There was no significant difference in specificity of these techniques: 96 , 94 , and 97 % respectively. In cases with histologically confirmed low grade urothelial carcinoma (LGUC) the sensitivity of cytological method was 20 % in conventional smears, 60 % in SurePath®, and 73 % in Cytospin-3. Specificity: 100 , 99 , and 94 % respectively.
Conclusion: Application of liquid-based techniques in urine sample cytopreparation allows to reduce research time and increases the diagnostical value of cytology

PS-19-006
The value of p16/Ki67 dual stain in Pap smears categorised as atypical squamous cells - cannot exclude high-grade squamous intraepithelial lesion (ASC-H)
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Objective: We evaluated outcomes of Pap smears diagnosed as ASC-H and assessed the value of p16/Ki67 dual stain in identification of women with subsequent biopsy-confirmed high-grade squamous intraepithelial lesions (HSILs).
Method: p16/Ki67 dual staining was performed retrospectively on the initial Pap cytology slides with ASC-H interpretation, gathered in a 36-month period. Results were compared to final histological diagnoses and/or cytological follow-up for at least 1 year.
Results: 169 cases fulfilled all conditions to be included in the study group. The rate of histologically confirmed HSIL was 57.4 %, of low-grade squamous intraepithelial lesion (LSIL) 17.7 % , and normal histology or follow-up was in 24.9 % of patients. Overall sensitivity and specificity of p16/Ki67 dual stain were 95 and 72 %, respectively. Overall positive likelihood ratio of p16/Ki67 in detection of HSIL was 3.41, considerably increasing pre-test probability from 57 % to post-test probability of 82 %.
Conclusion: A substantial subset of patients with ASC-H interpretations is associated with an appreciable risk of clinically significant cervical disease. p16/Ki67 dual stain can provide additional valuable information that may lead to higher quality management of women with ASC-H, especially when initial colposcopy or biopsy results do not show HSIL.

PS-19-007
Quality control of HPV test. Interlaboratory agreement of cobas 4800
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Objective: HPV test high sensitivity for CIN2+ is the basis for new cervical cancer screening protocols. Cobas 4800 is a FDA-approved HPV test for cervical cancer screening. It is based in a real-time PCR, detecting high-risk HPV and genotyping HPV 16, 18 and other high-risk HPV (HR-HPV) than HPV 16 or 18. Inter and intralaboratory quality controls are recommended. We report the results of a quality control program between three participating laboratories.
Method: All three participating laboratories chose 10 positive cases with a Ct<35 (P-A), 10 positive cases with a Ct > 35 (P-B, "grey zone") and 10 negative cases (N). The laboratories interchanged their cases between two laboratories a as ring. The laboratory agreement was measured.
Results: The agreement in N and P-A cases was 100 % .The agreement in P-B cases was 88.3 %. The agreement in HPV 16 and 18 was 100 % . The agreement in HR-HPV other than 16 or 18 was 88.3 %
Conclusion: Cobas 4800 has an excellent agreement between laboratories in negative, positive (P-A) and in HPV 16 and 18 cases. Discordant cases are located always in the (P-B, "grey zone") and in HR-HPV other than 16 /18.

PS-19-008
Atypical glandular cells in Pap smears: A retrospective study with histopathological correlation
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Objective: Although the atypical glandular cells (AGC) category is rarely diagnosed in Pap smears, early detection of this rare entity is crucial for patient management. The aim of this study was to evaluate the incidence and the significance of AGC detected in Pap smears.
Method: We retrospectively reviewed Pap smears diagnosed as AGC, between May 2011 and April 2016. The cytological features of atypical glandular cells in Pap Smears were recorded and cyto-histological correlation was evaluated.
Results: Among 61,334 Pap tests, 179 (0,29 %) cases were diagnosed as AGC. 123 of these cases which had concurrent biopsies were included in the study. Of 123 cases, Pap smears were diagnosed as AGC-NOS, AGC-favor neoplasia and adenocarcinoma in 60, 27 and 36 cases, respectively. The malignant histopathology was detected in 87 cases (70,7 %), including 40 cases (46 %) of endometrial, 28 cases (32.2 %) of ovarian, 13 cases (15 %) of cervical malignancies and 6 cases (6.8 %) of metastasis from other sites. Feathering, loss of polarity, overlapping, papillary pattern, three dimensional formation and nuclear irregularity were found statistically significant to determine malignancies ($p < 0.05$).
Conclusion: The results of this study suggest that in differentiation of histologically benign and malignant cases, the interpretation of architectural features of the glandular cells are more valuable than the abnormal nuclear features.

PS-19-009
Malignancy risk for the categories of respiratory cytology based on the standardised terminology and nomenclature of the Papanicolaou Society of Cytopathology (PSC): A retrospective study of Acibadem University School of Medicine
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Objective: The recently formulated nomenclature for respiratory cytology proposed by the PSC harbors a risk of malignancies for 6 categories,-namely- non-diagnostic (ND), negative for malignancy (NFM), atypical (A), neoplastic (N), suspicious for malignancy (SFM) and malignancy (M). To set up the rationale patient management and the decision of the requirement of re-biopsy were the main reasons for the propose of this classification system. The aim of this retrospective study, was to evaluate the risk of malignancies of the respiratory specimens' data of the Acibadem University, cytopathology subdivision based on the PSC guidelines.
Method: The cytopathology reports and pathology confirmations were reviewed for 1291 materials from 1019 patients between 2010 and 2016 years. The reports of cytology specimens including bronchial brushing, sputum, FNA leading by ultrasound, computerized tomography, endobronchial ultrasonography, bronchial lavage were separately reviewed and classified by the

currently accepted classification. Tissue biopsies were used as a gold standard to estimate the risk of malignancies which was available for 287 cytology samplings. Descriptive statistics were performed by Microsoft Excel 2011.
Results: 287 surgical follow up were obtained for 1291 cytology sampling. ND 16 %, NFM 53 %, A 5.4 %, N 0.4 %, SFM 2.1 % and M 23 % were of all data and the respective risk of malignancies for each category were 62 , 49 , 59 , 20 , 90 and 85 %. Sensitivity was 55 % and specificity was 84 % when categories A and N were excluded.
Conclusion: Despite of the slightly increased malignancy ratios of each category, the highest risk of malignancy was found in ND category based on the estimated values proposed in the PSC classification.

PS-19-010
Correlations between FNA cytology and histopathological diagnosis in breast cancer
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Objective: FNA is a cost-effective method of diagnosis in breast pathology and provides useful material for markers testing on cell blocks. Our comparative study was designed to evaluate the efficacy, diagnosis accuracy, and limits of FNA breast cytology versus histopathological examination.
Method: 89 cases of malignant breast tumours, with patients ages range between 40 and 83 years old, have been analyzed by FNA cytology, consecutive routine histopathology, supplemented by Her-2 and hormone receptors immunohistochemical evaluation, in 44 selected cases. Cytology grading has been independently performed by two histopathologists, by applying Hunt, Black, Fisher, Massod, Howell, Mouriquand, Robinson, Khan, and Taniguchi cytological criteria, followed by Nottingham criteria in histopathological specimens. The statistical analysis used Pearson's chi square test and Spearman's Rank.
Results: The accuracy of cytological diagnosis has been 98.88 %. The correlation between cytological and histopathological grading revealed a significant association (k = 0.592, $p < <0.01$, 95%CI, $\chi 2 = 15.35$, $p = 0.0041$, and $r = 0.739$, $p < <0.01$, 95%CI), with the highest correlation in Robinson system.
Conclusion: Our study revealed significant correlations between cytological and histopathological grading. Cytological grading limitations are related to in situ versus invasive breast carcinomas discrimination. The routine application of scoring system in FNA cytology could improve patients' prognosis, by fast track selection of high grade tumours for adjuvant therapies.

PS-19-011
The accuracy of p16/Ki67 dual stain in Pap smears in the detection of HSIL in women with positive self sampling HPV test
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Objective: P16/Ki67 dual stain in Pap smears has been proven as an effective method for reliably predicting HSIL by different studies. According to the manufacturer's instructions, the result is positive when p 16 and Ki67 immunoreactivity is simultaneously present within at least one cell in the smear.
Method: Seventy-two consecutive positive dual stain results in women with positive HPV self-sampling test were divided according to the number of positive cells into groups with 1, 2, 3, 4 and 5 or more positive cells. The outcome was compared to final histological diagnosis and was defined as clinically significant at the threshold of high-grade squamous intraepithelial lesion (HSIL).
Results: None of the patients with one ($N = 9$) or two ($N = 8$) positive cells had clinically significant histological diagnosis. Patients with three ($N = 3$) or four ($N = 3$) positive cells had HSIL in 33.3 %. 71.4 % of patients with five or more positive cells ($N = 49$) had histologically confirmed HSIL. These results were statistically significant at $p < 0.01$.
Conclusion: Our study demonstrated that accuracy of p16/Ki67 dual stain increases with the number of positive cells. Further studies and long-term outcome would be useful to clarify the importance of quantitative analysis of positive cells.

PS-19-012
Classification of nodal small cell lymphomas in cytopathology
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Objective: The diagnosis and classification of nodal small B cell lymphomas (NSBCL) in cytology is particularly challenging since different entities have similar morphology. Therefore, the determination of lymphoma cells' immunophenotype with flow cytometry (FC) is of paramount importance in classification of these neoplasms in fine needle aspiration biopsy (FNAB) samples.
Method: The expression of antigens CD10, CD5, CD23 and FMC7 determined with FC was evaluated on 152 FNAB samples of patients with primary histologicaly confirmed NSBCL.
Results: Correctly were classified 115 (76 %) cases: 94.3 % cases of chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL), 71 % mantle cell lymphomas (MCL), 69.1 % follicular lymphomas (FL) and 38.5 % nodal marginal zone lymphomas (NMZL). Typical immunophenotype according to the expression of CD5, CD10, CD23 and FMC7 antigens was found in 92.5 % CLL/SLL cases, 77.4 % MCL, 50.1 % FL and 23.1 % NMZL.
Conclusion: The results of our study confirmed that most cases of primary NSBCL can be correctly diagnosed and classified from FNAB samples when FC results and morphology are simultaneously taken into account. The proportion of correctly classified cases depends on the NSBCL type and is related to the proportion of cases with typical immunophenotype in each type of NSBCL.

PS-19-013
Granulocytes contacting with tumour cells of cultured cell lines, form of extracellular DNA networks creating favorable conditions for the vital activity of tumour cells
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Objective: It has been suggested that the extracellular DNA has neutrophilic origin and tumour cells stimulate the production of extracellular networks by neutrophils.
Method: To evaluate the viability and functional status of neutrophilic granulocytes in contact with in vitro tumour cells and compare impact of the modeled low intensity microwave solar radiation with the frequency range (4.0–4.3) GHz of electromagnetic radiation and modeled technogenic radiation with a frequency of 4.1 GHz on viability of continuous cell lines in case of larynx epidermoid carcinoma (hep-2 clone) both in isolation and mixed with neutrophilic granulocytes.
Results: In 24 hrs of incubation a significant increase of tumour cells, the presence of conglomerates, complexes and symplasts were registered. Apparently, such registered phenomenon is due to the shielding effect of neutrophil extracellular dna preserving the viability of tumour cells exposed to electromagnetic radiation of different origin and enhancing their proliferation.

Conclusion: With and without any type of exposure granulocytes contacting with tumour cells of cultured cell lines, form extracellular dna networks which wrap the tumour cells bringing them closer to each other, creating favorable conditions for the vital activity of tumour cells and contributing to the formation of complexes and symplasts, probably resulting in marked pro-oncogenic impact.

PS-19-014

Routine use of CellDetect for the identification of urothelial carcinoma in voided urine

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Objective: CellDetect histochemical stain uses a color feature to highlight neoplastic cells in urine specimens. A blinded study has recently shown the ability of CellDetect to accurately identify 78 % of low grade (LG) bladder cancer tumours in voided urine. The objective of the present study was to confirm this finding in routine clinical settings.
Method: Patients undergoing cystoscopic examination or TURBT were enrolled in this study. Collected voided urine samples were preserved, centrifuged twice and processed into two smears using a cytocentrifuge. Slides were stained automatically by CellDetect and Papanicolaou (Pap). A Cytopathologist, blinded to the final diagnosis, first observed the Pap slide and subsequently the CellDetect slide. The results were then compared to biopsy and/or cystoscopy.
Results: A total of 90 sets of urine smears, including 57 negative and 33 positive cases, were prepared. The overall sensitivity and specificity of CellDetect were 82 % and 86 % respectively compared to 58 % and 95 % for Pap staining. Notably, higher sensitivity of CellDetect versus Pap was observed for both LG + PUNLP (n = 17, 71 % versus 35 %, $p < 0.04$) and high grade tumours (n = 16, 94 % versus 81 %). When the patients were grouped by disease stage, higher sensitivity of CellDetect versus Pap was observed for both NMIBC (n = 24, 81 % versus 63 %) and MIBC (n = 9, 100 % versus 78 %).
Conclusion: This study validates the use of CellDetect in routine clinical settings and confirms its ability to accurately identify UCC throughout all cancer grades, particularly LGs. Additional study is underway to compare the performance of the test to that of FISH.

PS-19-015

Self-assessment-tests for the Eurocytology website

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Objective: To create the Self-Assessment-Tests (SATs) for the successfully updated Eurocytology website (Leonardo Eurocytology Project 2013–2015).
Method: The most important features of SATs in agreement with the contemporary theory of education, diagnostic practice, and board examination requirements were selected. Uniform structure (not length) of SATs was agreed upon.
Results: 1) Apparent differences were found when comparing the recent rules of creating SATs of American Society of Cytopathology and CY-test. 2) SATs based in their theoretical parts on the material of the Eurocytology chapter (only) were prepared for the first two chapters chosen (Pathology of Effusions, Pathology of Thyroid). 3) Microphotography cases with the typical features and histopathology verifications were based on slides provided for scanning. 4) Links to the particular chapter in the Cy-test for further extended testing were added.
Conclusion: The construction and evaluation of SATs represents a continual process to increase the quality of the updated website www.eurocytology.eu.

PS-19-016

Diagnosis of intrapancreatic spleens with fine needle aspiration: Revision of four cases

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Objective: The incidence of accessory intrapancreatic spleens is 20 % and 10 % of them are located in pancreatic tale. They are benign and usually asymptomatic. With radiological techniques, they can be confused with neuroendocrine tumours of pancreatic tale, wich are frequent.
Method: We revise four cases of tumours in pancreatic tale, between 2013 and 2017, which they appear to be neuroendocrine tumours radiologically and in which a FNA is done.
Results: The four cases, (three men and a women between 61 and 75 year old) were incidental tumours and located in pancreatic tale. In two of them, the lesion was discoverd with CT because of an hepatopathy, in other case, it was discovered with an urynary system ecography due to bladder incontinence and in the last one was discovered with CT after surgery because of a rectum adenocarcinoma T2N1. In all of them, we saw citologycally a polimorfous population of lymphocytes without atypias, which were CD20 and CD3 positive. CD8 was positive in endothelial cells of the sinusoids.
Conclusion: It's important to do a FNA when a pancreatic tale tumour is discovered incidentally because it allows us to distinguish a real tumour from an intrapancreatic spleen, before doing any surgical intervention.

PS-19-018

A multimodal approach to the diagnosis of pancreatic cysts at a tertiary hepatobiliary centre

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Objective: Pancreatic cysts are uncommon when compared with solid masses, accounting for only about 10 % of pancreatic lesions. Although many of these cysts are premalignant, not all require surgical intervention. The most important job of the cytopathologist is to distinguish non-neoplastic and benign neoplastic cysts that do not require surgery from neoplastic cysts that may need resection. Our aim was to assess the contribution of ancillary investigations and information to the diagnosis, comparing where possible with the clinical/surgical outcome.
Method: We reviewed all pancreatic cysts for which cytology samples were submitted to the Royal Free Hospital over a 3 year period. These were classified by condition, comparing site, radiology, biochemical tests (carcinoembryonic antigen and amylase) and outcome.
Results: Of the 242 cytology specimens there were 66 pseudocysts, 44 cases of IPMN, 40 cases of cyst NOS, 27 serous cysts, 14 mucinous cysts, 9 cases suspicious for malignancy, 6 cases of mucinous cystic neoplasia, and 9 cases classified as 'other' (including a solid pseudopapillary neoplasm and lymphocoele). 27 cases were deemed inadequate.
Conclusion: We strongly recommend the use of a multimodal approach in the cytological diagnosis of pancreatic cysts. This should include radiological appearance, biochemical investigations and multidisciplinary discussion.

PS-19-019

Cytological features of lymphoepithelioma-like carcinoma of the breast

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Objective: Lymphoepithelioma-like carcinoma (LELC) is exceptionally rare in the breast and, to our knowledge, there are only two case reports concerning the cytological findings. Herein, we examined characteristic cytopathological features of mammary LELC.
Method: The patient was a 50-year-old postmenopausal Japanese woman who had noted swelling of a left axillary lymph node. Ultrasonography revealed an irregularly shaped, hypoechoic left breast mass as well as enlargement of the regional node. Fine needle aspiration (FNA) of the affected lymph node yielded a cytologic diagnosis of metastatic carcinoma.
Results: The intraoperative FNA specimen from the breast tumour showed high cellularity with numerous lymphocytes in a hemorrhagic background. Carcinoma cells were loosely arranged in solid clusters, although single, dissociated carcinoma cells were frequent. Some carcinoma cell clumps were prominently infiltrated by lymphocytes. Large carcinoma cells had ovoid or irregularly shaped nuclei with a fine granular chromatin pattern and distinct nucleoli. Multinodular tumour mass, measuring 12x8mm, were histologically composed of polygonal carcinoma cells, with relatively clear cytoplasm and large nuclei, accompanied by intratumoural tumour-infiltrating lymphocytes (TILs) as well as stromal TILs. Metastasis was identified in one of 23 excised lymph nodes. Carcinoma cells were immunohistochemically positive for cytokeratin AE1/AE3 and 34βE12 showing a "triple negative" subtype. Epstein-Barr virus-encoded RNA in situ hybridization (EBER-ISH) was negative.
Conclusion: Cytological differential diagnosis of medullary mammary carcinoma requires recognizing lymphoepithelial clusters and fine nuclear chromatins. Recently, TILs have been demonstrated to predict a favorable outcome with responses to chemotherapy. It is, therefore, worth keeping in mind LELC when paraneoplastic lymphoid lineage cells are detected in cytologic smears. (Cytopathology. 2017; 28: 169–172)

PS-19-021

Expression of ki-67/p16 in normal, atypical and neoplastic cells in urine cytology

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Objective: to investigate the expression of the CINtecPlus (Roche) kit Ki-67/p16 in possible neoplastic urothelial cells in urine cytological specimens.
Method: urine cytological samples from normal controls (33), anonymous rest urine from samples diagnosed as suspicious or malignant (32), benign conditions (4), controls after treatment for UC (20) and newly diagnosed UC (30). Samples were fixed for 24 hrs in SurePath and then an unstained SP sample was prepared. Immunocytochemistry for ki-67/p16 dual staining kit was done on all specimens.
Results: 8 newly diagnosed UC (all high grade) and 6 anonymous specimens showed dual positivity. None of the low grade UC and the control specimens after treated UC showed dual staining. Only 15/86 symptomatic cases were negative for both markers, whereas 59/86 showed positivity for both but not dual staining. 27/86 cases were positive for ki-67 (22) or p16 (5). Normal controls and known benign specimens were negative for both markers.
Conclusion: Positivity for both markers without dual staining is common, but the diagnostic implication is so far uncertain. All normal controls and known benign conditions were negative for both markers. A minority of symptomatic samples was negative for both markers, but follow-up on these is still too short to make definitive conclusions. Dual positivity was only found in some of the high grade UC that were not a diagnostic problem. The findings indicate that negativity for both markers could be consistent with a benign cell material, whereas positivity for one or both needs further investigation.

PS-19-022

Feasibility of the CellDetect platform added on cytology for bladder cancer monitoring in a clinical setting

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Objective: In the bladder cancer monitoring, cytology (CYT) still plays an important role as a cost-effective, non-invasive urine test, however of limited validity. 'CellDetect (CellD), a new histochemical platform, is based on adding color discrimination to cytology. CellD combines a plant extract with generic stains and showed efficacy in multicenter trials. However, there is few data on test applicability in routine use.
Method: 47 patients monitored for BC recurrence were prospectively enrolled. Split-samples of voided urine obtained before cystoscopy were processed by cytospin and stained by either Papanicolaou or CellD. For both procedures, the cutoff for positive was "Suspicious". As CellD relies on both color and morphology, the impact of the CellD color alone was also determined.
Results: 21 patients showed recurrence (Ta/1/CIS/≥2 = 10/1/5/5, low/high grade = 12/9) while 12/14 cystoscopies/biopsies presented negative. Sensitivities/specificities/NPV/PPV/ accuracies for CYT and CellD were 42.1/92.0/80.0/67.7/70.5 % and 76.2/69.2/66.7/78.3/72.3 %, respectively. Sensitivities for low/high-grade BC were 16.7/71.4 and 50.0/100.0 % for CYT and CellD, respectively. Among the cases diagnosed exclusively based on CellD color (>70 %, $n = 28$), 15/19 (78.9 %) were true-positive and 5/9 (55.6 %) true-negative.
Conclusion: CellD clearly improved CYT performance in this clinical setting. The request to the manufacturer now is to develop a more easy-to-handle procedure suitable for the laboratory daily practice. In addition, an evaluation of the test in the pure target population (cystoscopies only) is warranted.

PS-19-023

Sensitivity of liquid based automated screened cytology. An estimate analysing 15518 database cases from an opportunistic screening population

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Objective: To analyse the sensitivity of liquid-based automated cytology in a of an opportunistic cervical cancer screening population of women from an area of 300.000 inhabitants of Barcelona (Catalonia, Spain).
Method: ThinPrep and Imaging System (Hologic) were used. A retrospective cohort study of women without previous cervical lesion or hysterectomy who had 2 or more cervical smear tests, between 2008 and 2012 was studied. Follow-up data including cytologic and histologic diagnosis. were collected The worst diagnosis in histology (in any biopsy or conization) was considered the gold standard result.
Results: A total of 15518 women were included. Most patients were Spanish (70 %). Mean age at the first cytology was 38 years (18–79). Eighty-three per cent cytology results were NILM, 6.7 % ASCUS, 8.2 % LSIL and 1.9 % HSIL. Mean and median time between cytology and biopsy was 113 and 71 days. Histology was available in 1018 cases: 361 negative (35 %), 394 CIN1 (39 %), 188 CIN2-3 (19 %) and 75

Carcinoma (7 %). Cytology sensitivity depending on cut-off was 40.5 % for CIN2+, 66.5 % for LSIL+ and 83.5 % for ASCUS+
Conclusion: Liquid based, automated screened cytology taking ASCUS as the cut-off, showed a high sensitivity (83.5). Cases with no follow-up in our area may bias these results.

PS-19-024
Fine needle aspiration cytology and correlation with transthorasic tru-cut biopsy results in lung masses
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Objective: The aim of this study is to compare the diagnostic yield of transthorasic fine needle aspiration (FNA) and tru-cut biopsy methods, which are commonly used for evaluation of lung masses.
Method: Cytological (FNAs and cell blocks) and tru-cut biopsy samples of 80 lung lesions, which were carried out at the same session, were compared. On-site cytological evaluation was performed for most of the cases.
Results: Among 80 cases, 58 (72.5 %) were malignant, 6 (7.5 %) were suspicious for malignancy, 12 (15 %) were benign, and 4 (5 %) were non-diagnostic by cytology results. When only tru-cut biopsy results were taken into account, 53 (66 %) were malignant, 1 (1.5 %) was atypical, and 26 (32.5 %) were benign. Of the 80 cases, 51 (64 %) had compatible cytology and biopsy results. In 16 cases (20 %) tru-cut biopsy was superior to cytology, while in 13 cases (16 %) cytology was superior.
Conclusion: FNA cytology is an effective method in assessing lung masses. Most of the time correct diagnosis can be made by cytology alone. Diagnostic yield of FNA cytology will be increased when both techniques are combined.

PS-19-025
Fine needle aspiration of a anaplastic carcinoma of the thyroid with TTF-1 and thyroglobulin expression on cervical metastasis: A case report
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Objective: Anaplastic carcinoma of thyroid (ACT) characteristically lacks immunohistochemical markers of thyroid origin. Most patients present with advanced disease and have very low survival rate.
Method: Sixty-four year-old man presenting with recent cervical mass and thyroid nodule. Both were submitted to fine needle aspiration cytology (FNAC). MGG and PAP stained smears and immunocytochemistry were performed.
Results: Smears of thyroid and cervical mass showed single cells and three dimensional aggregates. Cells were round and spindle, with large pleomorphic nuclei, bi/multinucleation, and dense cytoplasm. Expression of TTF-1 and thyroglobulin was strong and diffuse on both samples. Cytokeratin and p53 were also focally positive. Despite the diagnosis of ACT, the patient was considered eligible for surgery. Histology confirmed cytological findings. Local recurrence was detected 1 month later and palliative radiotherapy initiated. The patient died 3 months after initial diagnosis.
Conclusion: TTF-1, PAX8 and TTF-2 are fundamental for differentiation of thyroid tissue and control expression of thyroglobulin, which has been linked to iodine avidity. As such, this expression is typically lost in ACTs although it has been reported in rare cases, as a result of diffusion from normal follicles. Our case expressed TTF-1 and thyroglobulin in both primary and metastatic tumour. However prognosis seems similar to classical ACTs.

PS-19-026
There is still a role for cytology in the "liquid biopsy" era?: A case of a patient showing adenocarcinoma to squamous cell carcinoma (SCC) transition during target therapy
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Objective: Non-small cell lung carcinoma harbouring epidermal growth factor receptor (EGFR) mutation, usually progress after an initial response to tyrosine-kinase inhibitors (TKI) treatment. Liquid biopsy enables with a simple blood draw the accurate detection of EGFR p.T790M mutation, the most common resistance mechanism, avoiding the more invasive tissue re-biopsy. However, in a subset of cases resistance mechanisms are more complex featuring both genetic and morphological changes.
Method: Here we report the case of a 67 years-old woman, affected by an EGFR mutated lung adenocarcinoma and treated by TKI. At disease progression, the patient developed a lymph node metastases showing morphological transition to squamous cell carcinoma which maintained the original EGFR mutation and developed an additional PIK3CA p.E542K mutant subclone.
Results: Tissue re-biopsy by the means of a minimal invasive fine needle aspiration cytology, provided an overall assessment of both morphology and genetic resistance mechanisms.
Conclusion: This case illustrates that there is still a role for cytology in monitoring targeted treatment response, even in the "liquid biopsy" era.

PS-19-027
Urinary WT1 positive cells as a non-invasive biomarker of crescent formation
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Objective: The purpose of this study was to assess the relationship between urinary WT1-positive cells (podocytes and active parietal epithelial cells) and WT1-positive cells in renal biopsy to investigate whether urinary WT1-positive cells are useful for detection of crescent formation.
Method: Fifty-two patients with kidney disease were investigated (15 cases with crescentic lesion and 37 cases with non-crescentic lesion) for immunoenzyme staining using anti-WT1 antibody for urine cytology and renal biopsy. Numbers of WT1-positive cells in urine and renal biopsy were counted, respectively.
Results: There was no correlation between urinary WT1-positive cells and WT1-positive cells in renal biopsy. However, the number of urinary WT1-positive cells in patients with crescentic lesion was significantly higher than in patients with non-crescentic lesion. In addition, the best cut-off value to detect patients with crescentic lesions using urinary WT1-positive cells was 5/10-mL (AUC = 0.735).
Conclusion: The results of our study suggest urinary WT1-positive cells can be used to detect patients with crescentic formation using a 5/10-mL cutoff value.

PS-19-028
Our experience with THY3a and THY3F thyroid cytology reporting
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Objective: Fine needle Aspirate (FNA) is the standard approach to thyroid nodules. Five, Royal College of Pathologist diagnostic categories are recognized (THY1-THY5). Up to 30 % of thyroid FNA have an

indeterminate report (THY3a and THY3F) Our aim is to compare "indeterminate" FNA and subsequent histological diagnosis on surgical specimen when available.
Method: We reviewed a consecutive series of FNA performed between January 1, 2016 to January 1, 2017. Positive Predictive Value (PPV) of malignancy and neoplasm determined.
Results: THY3a (28) and THY3F (30) with known follow-up. PPV for THY3a was 65 % (15/23) for neoplasm and 21 % (5/23) for malignant tumour. In the THY3F category the PPV for neoplasm was 80 % (24/30); PPV value for malignancy was 27 % (8/30).
Conclusion: Our THY3a PPV for malignancy of 21 % in cases with proven histology is higher than 17 % reported by the RCPath. Our THY3f the PPV for malignancy (27 %) is in the range of the up to 40 % reported by the RCPath. This study confirms high diagnostic accuracy in FNA reporting for thyroid cytology but also indicate the need to develop additional tests such as multigene-next generation sequence (NGS) assays to increase the PPV for malignancy in category THY3a and THY3f.

PS-19-030
Endoscopic ultrasound-guided fine needle aspiration cytology of gangliocytic paraganglioma of the duodenum
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Objective: To describe the cytological findings in one case of duodenal gangliocytic paraganglioma evaluated by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) and review the literature.
Method: A 60-year-old male followed because of mucinous adenocarcinoma of the colon treated with total colectomy and chemotherapy. CT-scan revealed a 5 x 5 x 3 cm solid duodenal mass and implants in left iliac fossa. Ultrasound-guided fine needle aspiration cytology (EUS-FNAC) was performed. The patient underwent partial duodenomectomy and implants resection.
Results: Smears showed a moderately-cellular population composed by medium-to large epithelioid and ganglion-like cells with pleomorphic nuclei and prominent nucleoli together with fusiform cells, single and in syncytial aggregates that incorporated metachromatic, fibrillary matrix. Neither necrosis nor mitoses were identified. Histological and immunohistochemical examination confirmed the cytological diagnosis.
Conclusion: Due to its rarity, the cytological descriptions of gangliocytic paraganglioma are still scarce. A mixed population of epithelioid, gangliocytic-like cells and fusiform cells, single or in syncytial aggregates with metachromatic fibrillary matrix should consider its diagnosis. Immunocytochemistry is required to achieve a correct characterization and distinguish it from well-differentiated neuroendocrine neoplasms, mesenchymal gastrointestinal tumours, metastatic carcinoma and melanoma. EUS-FNA is an excellent procedure for the initial approach of this neoplasm of uncertain histogenesis.

PS-19-031
Different types of neoplasms detected on Pap smear
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Objective: The majority of cervical cancer cases according histological type are squamous cell carcinoma, less adenocarcinoma and the remainder are other epithelial tumours or other malignancies. The aim of this study is evaluation of the different types of malignant neoplasms detected on Pap smear.
Method: We retrospectively analyzed 29 cases of malignant neoplasm detected on Pap smear. All of them were reported in our institutions during the period of 3 years. These neoplasms were histologically confirmed.
Results: All 29 operated patients underwent previous biopsy and/or endocervical curettage. Age distribution was between 3 and 75 years. Squamous cell carcinoma was the most frequent type of cervical carcinoma according the 22 cases (75,9 %). There were 4 cases (13,8 %) of adenocarcinomas of which one was endocervical type of mucinous adenocarcinoma, one was serous adenocarcinoma and two cases of endometrioid adenocarcinoma. From the group of other epithelial tumours we detected one case of adenosquamous carcinoma. There was one case of malignant mixed mesodermal tumour of endometrium that extends into the endocervix. In the evaluated group there was one case of germ cell tumour of the ovarium (Yolk sac tumour) in 3 years old patient. Tumour infiltrated the wall of the vagina and was detected on Pap smear.
Conclusion: Although Pap smear is used for detecting precancerous lesion and cancers of the uterine cervix, carefully examination should be done because Pap smear can be used like diagnostic tool in detecting tumours of other parts of the genital tract.

PS-19-032
Cytologic diagnosis of mammary secretory carcinoma
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Objective: Secretory carcinomas account for < 0.15 % of all breast cancers .The tumour is seen usually in childhood but can also ocur in adults.This low grade breast carcinoma has distinct features of histology and cytological diagnosis is challenging.
Method: Sixty-three year-old female patient presented with 10x11mm, round, well demarcated breast mass. A fine needle aspiration biopsy was performed.Mammography results were within normal limits.
Results: Cytologic preparations and sections from cell block revaled generally cohesive , occasionally discohesiv crowded ductal cells with oncocytic change in eosinophilic secretory background. Intracytoplasmic vacuolization was detected. Myoepithelial cells were not identified among tumour cells. There were also some micropapillary structures. On immunhistochemistry of the cell block,these cells were negative for estrogen receptor, progesterone receptor and androgen receptor but positive for S100. It was diagnosed as atypical aspirate with suspicion of secretory carcinoma. Patient has directly undergone mass excision.Histologic diagnosis was mammary secretory carcinoma.
Conclusion: Mammary secretory carcinoma is a very rare tumour and it may be challenging on cytologic diagnosis.

PS-19-033
Cytological diagnosis of breast implant associated anaplastic large cell lymphoma, a case report and literature review
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Objective: Breast implant associated anaplastic large cell lymphoma (BI-ALCL) is a usually indolent disease with an incidence of 0,3 per 100000. We present the first case diagnosed in our institution by fine needle aspiration (FNA).
Method: 59 y/o patient who developed seroma 16 years after reconstructive surgery after bilateral mastectomy. FNA was performed.
Results: Cytology smears show atypical large lymphoid cells, some with horseshoe-shaped nuclei and prominent nucleoli, intensely expressing CD3 and CD30 while being negative for CD20, TIA1 and ALK. Ki67

proliferative index is high. Flow cytometry is compatible with anaplastic T-cell lymphoma. Capsulectomy was performed including both breast prostheses and mastectomy scars. No evidence residual malignancy. The patient is considered in complete remission 8 months after diagnosis.
Conclusion: BI-ALCL is an infrequent entity, with 258 cases in the most extensive review found in the literature, where only 5 died. It should be suspected in patients with periprosthetic seroma appearing after 1 year after implantation, forcing cytological analysis. Cytology is a reliable tool for the diagnosis and monitoring, and sometimes more sensitive than the histological analysis. Cytological findings allow an accurate diagnosis, enabling appropriate treatment at an early stage where surgical resection is the treatment of choice, and is sufficient in most cases.

PS-19-034

Diagnostic accuracy of fine needle biopsy cytology of thyroid nodules at a specialised clinical centre in Bulgaria for a period of 20 years

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Objective: The aim of this study was to evaluate the diagnostic accuracy of fine needle biopsy cytology (FNBC) of thyroid nodules at our institution for a period of 20 years.
Method: A retrospective analysis of cytological results of all patients who underwent thyroid FNB (n = 8287) for the study period (1996–2015) was done. They were categorized into 5 categories: non-diagnostic-3.2 %; benign-82 %; indeterminate (follicular proliferations)-4.3 %; suspicious for malignancy (SFM)-6 % and malignant-4.5 %. Histological follow-up was available in 726 cases (195, 79, 248 and 204 patients with benign, indeterminate, SFM and malignant FNBC, respectively).
Results: The overall malignancy rate on final histopathology was 66 % (n = 477) and PTC was the most commonly diagnosed - in 95 % (n = 449), especially papillary microcarcinoma (n = 254). The correlations between the benign, indeterminate, SFM and malignant categories and histology showed that the histological malignancy rates were 7 %, 52 %, 89 % and 99 %, respectively. After exclusion the cases with indeterminate cytology, the specificity, sensitivity, positive and negative predictive values, as well as diagnostic accuracy, were 97 , 86 , 94 , 93 and 94 %, respectively.
Conclusion: Our results showed that FNBC is a sensitive, specific and reliable diagnostic method for evaluation of patients with thyroid nodules, but knowing the limitations of thyroid cytopathology in cases with follicular-pattern lesions is of importance.

PS-19-035

Usefulness of fine needle aspiration in diagnosis of primary lymphoma of the eye and ocular adnexa. Sample optimisation and accurate diagnosis. Is biopsy always necessary? Case report and literature review

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Objective: Primary lymphomas of the eye an ocular adnexa are very rare neoplasms. These represent less than 2 % of non-Hodgkin's lymphomas. Its incidence is higher in women and patients over 50 years. Given the location and tumour size, core needle biopsy is not always possible, so it is postulated the use of fine needle aspiration (FNA) as an optimal technique for its diagnosis.
Method: Eighty-six years old male patient, with a left upper eyelid mass - 2 years slow growth- hinders the opening of the eye. Imagen study (CT SCANNER - NMR) was performed: 33 mm intraorbital mass. Ultrasound FNA performed by cytopathologist was made.
Results: At Giemsa and H&E smear an atypical monomorphic lymphoid population was observed. On cell block immunohistochemical staining were carried out. Immunohistochemical profile was compatible with low grade B lymphoma, supported by flow cytometry study.
Conclusion: FNA combined with complementary techniques such as flow cytometry and sample optimization -immunohistochemistry on the cell block-, were enough to make a precision diagnosis, allowing effective treatment to be established, without the needed for further expensive/ bloody studies as core needle biopsy. The patient underwent radiotherapy with 2 years follow up disease free.

PS-19-036

A rare case of urine cytology from recurrent urothelial carcinoma with extensive squamous differentiation mimicking conventional squamous cell carcinoma (SCC)

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Objective: Although the urine cytology was essential for the detection of primary urinary neoplasia, it can provide additional diagnostic information; however, in some cases, can be a diagnostic confusion, especially squamous cell lesion from the female patients. We report a rare case of recurrent urothelial carcinoma (UC) with extensive squamous differentiation in urinary bladder, mimicking squamous cell carcinoma.
Method: A 72-year-old female, had a previous history of transurethral resection (TUR) for H-G papillary UC of urinary bladder (UB) 4 years ago; followed by three times of recurrent UC. After the last TUR, 3 times sequential urine cytology analyses were performed; last two cytologic evaluations revealed atypical squamous cells with scattered dyskeratotic and tadpole-appeared cells; the cytologic diagnosis was compatible with squamous cell carcinoma.
Results: The resected UB showed an ill-demarcated, whish gray, irregularly exophytic and infiltrative mass, on the left lateral wall of UB. Microscopic features were of conventional squamous cell carcinoma, moderately differentiated; furthermore, there were microscopic foci showing obvious urothelial differentiation. In each of initial and sequential recurrent tumours, none of them were detected in HPV typing assay.
Conclusion: Squamous differentiation is the most common variant histology in UC. It is usually associated with specific molecular changes, different from those of conventional UC; and has often aggressive behavior. The role of HPV in the pathogenesis of squamous cell carcinoma of UB or UC with squamous differentiation remains uncertain. Interestingly, several studies showed p16 expression was not correlated with the presence of HPV infection in squamous cell carcinoma in UB.

PS-19-037

Cytologic detection of recurrent extramammary paget's disease of the vulva: A report of a case

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Objective: Extramammary Paget's disease of the vulva (EMPDV) is a rare form of skin cancer. We report a case of EMPDV in which cytologic study rendered early detection of recurrent disease in an asymptomatic patient.
Method: Vaginal Papanicolaou smear was taken in a 75 year-old woman, who had EMPDV 5 years before. No specific complaint such as pruritus or pain was reported. Three years prior to the admission, recurrent EMPDV was confirmed by punch biopsy and excision of the vulva was performed a year later. Invasive carcinoma was present as well as Paget's disease (4 mm of depth) and inguinal lymph node showed metastatic tumour. The patient underwent radiotherapy.

Results: Slides of liquid based preparation showed hypercellular smear with numerous abnormal cells in clusters or in isolated forms. Pattern of "cell within cell" (pseudocannibalism) was occasionally present. Cells were large, polygonal with increased N:C ratio, occasionally binucleated and with macronucleoli. Cytoplasms were variable from pale and delicate to dense or basophilic. Vacuolated cytoplasm were common. Abnormal cells were immunoreactive for cytokeratin 7 and BRST-2.
Conclusion: Recurrent EMPVD of the vulva after surgery can be easily and efficiently detected by vaginal smear especially when the identification of the exact lesion is not easy.

PS-19-038
Fine-needle aspiration cytology of Merkel Cell Carcinoma: A report of two cases
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Objective: Merkel cell carcinoma (MCC) is a neuroendocrine tumour that occurs frequently on the head and neck. It usually originates in the dermis, but in rare instances it has arisen in other primary sites, including the oral mucosa and the parotid gland. Fine-needle aspiration cytology (FNAC) of MCC has been described rarely in the literature.
Method: We report the first case of a 66-year-old male patient who presented with a 2-cm diameter swelling in the parotid gland and the second case of a 87-year-old female patient who presented with a 6-cm diameter lymph node in the upper cervical region. An ultrasound guided FNA was performed in both.
Results: Highly cellular both aspirate containing numerous loosely cohesive and dispersed malignant cells with scanty cytoplasm and nuclei with inconspicuous nucleoli showing moulding and smear artefact. For the differential diagnosis immunohistochemistry was performed on cell blocks. Perinuclear "dot-like" cytokeratin 20 (+) / perinuclear "dot-like" cytokeratin (+) / chromogranin (+) immunophenotype was identified in both cases.
Conclusion: MCC is often an aggressive tumour with high tendency for local recurrence, lymph node involvement and distant metastases. So it should be included in the differential diagnosis of malignant round blue cell tumours.

PS-19-039
Primitive neuroectodermal tumour of uterus in Pap Smear: A case report
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Objective: Primitive neuroectodermal tumours of uterus are extremely rare female genital tract neoplasms. A 37 year old women gravida 4, para 1 was referred to our Department of Gynecology and Obstetrics from a local medical center and presented with a two-month history of vaginal bleeding. Transvaginal ultrasonography revealed a 95 x 35 mm mass in the uterine cavity and an endometrial biopsy was performed at another center. The biopsy was reported as malignant tumour infiltration presumed to be an endometrial origin.
Method: In our clinic, PAP smear was performed.
Results: In Pap Smear, tumour cells were arranged as multiple clusters. These groups were composed of cells with scant, round and vacuolated cytoplasm and a high N/C ratio. Whereas some tumour cell nuclei had basophilic- finely granular chromatin with prominent nucleoli, others included only eosinophilic- fine chromatin. In both cell types, the nuclei were round-to oval,hyperchromatic and had smooth nuclear membrane. After Pap Smear was reported as malignant tumour cells, the patient underwent a radical hysterectomy, bilateral salpingo-oophorectomy and omentectomy and final pathology report revealed PNET. The patient is alive in five-year follow up.
Conclusion: Although tumour cells of PNET rarely present in Pap Smears, sometimes they can be the first sign and lead to a guide for management of patients.

PS-19-040
Thyroid secondary tumours diagnosed by FNA: 6-year-experience from tertiary care centre
I. Kholova*
*Fimlab Laboratories, Pathology, Tampere, Finland

Objective: Secondary tumours in the thyroid gland are rare. Thyroid fine-needle aspiration (FNA) is useful in nodule evaluation. The goal was to examine the cytological and clinical features of secondary tumours diagnosed by FNA.
Method: A series of 15 secondary tumours from the 6-year-period (2011–2016) from university hospital pathology department is presented.
Results: The secondary tumours were diagnosed in 7 males and 8 females with mean age 71 years (age range 47–95 years). The primary malignancy was known in 10 cases in time of FNA diagnostics. The cell block was performed in 13 cases with contributive immunocytochemistry in 10 cases. The histopathological correlate was available in 5 cases, where surgical resection of thyroid gland or autopsy was performed. In two cases, continuous spread of primary tumour was revealed.
Conclusion: FNA is reliable in the diagnostics of thyroid secondary malignancies with the contributive role of immunocytochemistry and essential role of the knowledge of malignancy history.

PS-19-043
Fine needle aspiration of synchronous bilateral breast cancer
E. Konstantinou*, S. Divani, M. Tzikopoulou, G. Kalodimos, A. Fericean, S. Rousogiannis, A. Vardouli
*General Hospital of Volos, Cytology Dept., Greece

Objective: Synchronous bilateral breast cancer is defined as two or more tumours which are distinct from each other and neither can originate from other tumour metastasis. Fine Needle Aspiration of breast lesions is routinely performed in our hospital. We reviewed our archives, found the diagnosed cases of bilateral breast cancer, and compared them with histologic findings.
Method: One thousand sixty-four aspirates in breast lesions, most of them palpable, were performed during the last 8 years. The aspiration was done using 21-gauge needle. Conventional and Thin Prep smears were prepared.
Results: Two hundred twenty-five were carcinomas. In seven women (mean age 65 years), the aspiration of the masses revealed bilateral carcinomas and excision was advised. All but two were palpable and in the latter cases an ultrasound guided FNA of the impalpable lesions was performed. The most common type was ductal carcinoma in both breasts.
Conclusion: A bilateral breast cancer is considered synchronous, by most authors, if it is diagnosed within 3 months after the first breast cancer. The initial tumour is usually diagnosed by palpation whereas the contralateral tumour is often diagnosed by mammography. Thus careful screening of the contralateral breast is essential in all patients with unilateral breast cancer.

PS-19-044
Diagnostic effectiveness of cell block preparation in routine thyroid cytology
U. Aykutlu*, Z. E. Yildirim, A. Veral, D. Nart
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Objective: The aim of this study was to determine the utility of cell blocks (CB) in the diagnosis of thyroid cytology.
Method: Over a period of 3 months, 468 cases underwent ultrasound guided thyroid fine needle aspiration, conventional cytology, liquid-based cytology (LBC) and CB evaluation. CBs were prepared from the residual aspirate LBC boxes. The contribution of the CB findings to the final diagnosis was assessed.
Results: Conventional cytology and LBC results were as follows: Bethesda I, %14.4 (n = 81); Bethesda II, %74,2 (n = 416); Bethesda III, %4,6 (n = 26); Bethesda IV, %1,2 (n = 7); Bethesda V,% 2.5 (n = 14), and Bethesda VI, %2,8 (n = 16). After combined cytological and CB evaluation, overall 60 cases (%10,7) final diagnosis has changed regardless of Bethesda category.Initially cytological diagnosis was non-diagnostic (Bethesda I) in 81 cases. CB changed the impression in 43 cases (%53) and this change was statistically significant ($p < 0.001$).Initially cytological diagnosis was AUS/FLUS (Bethesda III) in 26 cases. After addition of CB findings, 6 cases diagnosis has changed ($p < 0.001$).
Conclusion: The contribution of the CB in the diagnosis of thyroid lesions are striking. Specifically, the samples that benefited most were initially non-diagnostic specimens and selected cases of AUS/FLUS while benign samples gained little additional information.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-20 History of Pathology

PS-20-001
Impact of Leningrad/Petersburg school upon pathology of respiratory infections
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Objective: Respiratory viral and bacterial infections still play an important role in morbidity and mortality all over the world, but in the literature the peculiarities of lesions due to single pathogen are very scare. The results of studies provided by V.D. Zinserling (1891–1960) and A.V. Zinserling (1923–1995) in Saint-Petersburg, Russia are not well known in world literature due to objective reasons.
Method: Analyze the results of long term studies of their scientific school and reveal the original concepts still being of high value.
Results: Main statements in the V.D. Zinserling' s doctrine of pneumonias (primarily formulated in 1939): in typical cases there is distinct correlation between etiology and pathological pattern of pneumonias; pneumonias due to pneumococci, staphylococci, streptococci, haemophilus have their peculiarities; croupose pneumonia is always caused by pneumococci, the so called stages in hepatization according to Carl Rokitanski are only variants of the disease. A. Zinserling described as the first (or partly seriously specified) the microscopical changes in influenza, parainfluenza, respiratory-syncytial, mycoplasma and chlamydial infections allowing preliminary evaluation of etiology; developed the concept of clinical importance of mixed infections in lesions of lungs and other organs.
Conclusion: The result obtained by Zinserling's scientific school has to be taken in consideration nowadays.

PS-20-002
Learning to observe. Observing to learn. The antique dermatological waxes of the Pathology Museum of the University of Florence
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Objective: IIn the past centuries, the making of wax moulages was an exclusive and sought-after art that was primarily used for teaching anatomy and pathology. Dermatology has benefitted from wax duplicates, which are not only tri-dimensional but also offer the "dimension" of colour, an essential element for a correct gross diagnosis. The Pathology Museum, part of the Museum of Natural History of the University of Florence, houses anatomical specimens and more than a hundred waxes of astounding beauty, almost photographic reproductions of the most common diseases in the nineteenth century, when the collection was set up.
Method: The original Catalogue of the museum was perused for moulages depicting skin diseases, together with their relevant clinical and/or autopsy findings.
Results: The wax collection of the Pathology Museum includes 29 dermatological models such as papulo-squamous disorders as well as infectious and neoplastic diseases.
Conclusion: The collection of skin moulages of the University of Florence constitutes a precious historical heritage of high scientific and artistic value. Silently but loudly, these models also introduce visitors to the dramatic psycho-social consequences of defacing diseases, still a difficult task for the contemporary physician.

PS-20-003
On moral and political philosophy of pathology in context of UNO-Agenda 21
E. Neu*, M. C. Michailov, U. Welscher, G. Ernst, T. Senn, C. Lütge, I. Ivanova, M.-L. Gräfin von Brockdorff, A. Hofstetter, E. R. Weissenbacher, J. Foltinova, V. Foltin, M. Schratz, G. Weber
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Objective: Pathology is a-priori central biomedical-discipline with moral&scientific responsibility counteracting disastrous health-situation of humanity&ecological-destruction.
Method: see Ref. IAP-2016 Köln Eur.J.Pathol. 469:S1 PS-20-007. Philosophy: IUPsyS-2008-Berlin IntJPsychol 43:154/248/615/799.
Results: CONCEPTION: Pathology is to be discussed in context of humanization/higher-effectiveness, interdisciplinarity. a. Foundation of departments for philosophical-pathology and integration in education&research. b. Foundation of national-continental-international pathol.-institutes via network of selected countries related to international-universities by G.MENSCHING & B.RUSSELL/Nobel-Laureate. c. Implication of pathological topics to intern. congresses for philosophy-FISP/psychology-IUPsyS/physiology-IUPS/biophysics-IUPAB/chemistry-IUPAC, also clinical-medicine: IUPHAR/FIGO/ISIM/ISR/SIU/etc. d. Enlargement of International Academy for Pathology/IAP by (sub-)continental/African-American-Australo-Asian/Chinese-Indian-European-national branches of IAP, independently from pathological-societies. Fundamentals for a-d conc. pathology: 1. International educational/research-programmes. 2. Common administration&laboratories. 3. Recognition of participants as intern./continental professors/doctors-etc./EU-UNO-employees? 4. Possibility for work in IAP-institutes/branches. 5. Regular successive financial-support for participants/projects by nat.-ministries/industry/Eur.-Union/UNESCO-etc. 6. Possibility for whole-life-work after 60 years as senior-scientists incl. honorary-professors&institut-directors-etc.
Conclusion: Implication of a-d&1-6 in pathology will help UNO-Agenda21 for better health&education in all countries. Support of IAP conc. proposals by governments-foundations-EU-UNESCO-WHO is necessary.

PS-20-004
The questionnaire portraits of five Russian pathologists
A. Zubritsky*
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Objective: This work has the aim to collect and systematize the biographical information on Professor Alexander Mikhailovich Vavilov, Professor George Gerasimovich Avtandilov, Professor Ippolit Vasilievich Davydovsky, Mikhail Fyodorovich Glazunov and Professor Oleg Konstantinovich Khmelnitsky.
Method: According to the questionnaires prepared by me.
Results: no
Conclusion: Professor Alexander Mikhailovich Vavilov, Known Russian scientist-dermatopathologist (22.04.1938 - 02.10.2007): Born in Moscow in a family of employees. Married. Having children. Graduated from the 2nd Moscow Medical Institute named after Nikolai I.Pirogov (1963). Defense of doctoral thesis on "Clinic, morphology and histogenesis of tumors of skin appendages (sweat glands and hair follicles)" (1990). Senior, leading researcher, Head, Department of Pathomorphology, Central Research of Skin and Venereology named after VG Korolenko ((1986–2007). He belongs to the development of clinico-morphological classification of skin lymphomas based on the phenotypic characteristics of B- and T-cell skin lymphomas. Research interests: Dermatooncology, immunomorphological studies of the morphology and morphogenesis of chronic dermatoses, the study of stromal-epithelial interactions in a number of keratodermias. The author of over 150 scientific works, including manuals for doctors "Pathomorphology of skin diseases", as well as chapters of "Skin Disease" in the reference book "Pathology" (2002). Distinctive feature: Modesty, intelligence, compassion, unselfishness and kindness, always ready to help and love to his family. He died in Moscow at the 70th year of life.
Professor George Gerasimovich Avtandilov, Well-known Russian scientist pathologist-morphometrist of the academician of the Russian Academy of Natural Sciences (21.09.1922 - 14.12. 2009): Born in Kizlyar, Terek region in the family of a doctor. Military service: captured, concentration camp Lamsdorf No.318 (1941–45); released from captivity (17.03.1945), the participant of the Great Patriotic War. Graduated from North Ossetian Medical Institute (1951). Doctoral thesis on theme "Dynamics of morphological changes and pathogenesis of atherosclerosis of the aorta and coronary arteries of the human heart (biometric study)" (1965). Head and creator of the first laboratory of Morphometry and Biophysics, Institute of Human Morphology, AMS of the USSR (1965–75). Head, Department of Pathology, RMAPE (1975–2009). Expert and temporary adviser for WHO in preparing ICD-9, ICD-O and the Centre for the study of kidney diseases; founded a new scientific direction—mathematical pathology on the basis of the use of computerized morphometric techniques and created a domestic school of quantitative pathological anatomy. Honored worker of science (1991) and the main pathologist of Ministry of Health of the RSFSR (1980–90). Author of over 400 scientific works, including 20 monographs and manuals, 15 inventions, 3 discoveries, and more. Hobbies: Classical symphonic music. He died in Moscow at the 88th year of life and was buried in the Armenian cemetery
Professor Ippolit Vasilievich Davydovsky, outstanding Russian scientist-pathologist, academician of the Academy of Medical Sciences of the USSR (01.08.1887 - 11.06.1968): Born in Danilov, Yaroslavl province, in the family of a local priest. Graduated from the medical faculty of Moscow University (1910). Doctoral thesis on "Morbid anatomy and pathology of typhus" (1921). Head, Department of Pathology, 2 Moscow Medical Institute (1930–68). Head, Laboratory of Pathology of Old Age, Institute of Human Morphology, AMS of the USSR (1961–68). One of the founders of the clinico-anatomical direction in the patanatomy and one of the best biopsists of the 20th century, rebuilt the teaching of private patanatomy and began to present it according to the nosological principle. Honored scientist of the RSFSR (1940); Chief pathologist of the evacuation hospitals (1941–45); Hero of Socialist Labor (1957). Research interests: Infectious diseases, atherosclerosis, pathology of combat injuries and wound complications, etiology and pathogenesis, questions of cellular pathology, organization of the autopsy cases in USSR, gerontology, general pathology and philosophical issues of medicine. Author more than 260 scientific works, including fundamental and original manuals and monographs. Distinctive feature: Punctuality, paradoxical thinking, very modest and accessible to all doctors. Hobby: Hunting. He died in Moscow at the 81st year of life from stroke and was buried in Novodevichy cemetery.
Mikhail Fyodorovich Glazunov, Russian pathologist-oncologist, scientist and educator (12.11.1896 - 11.11.1967): Born in Tsarskoye Selo near St. Petersburg in family of manager of St. Petersburg branch of chocolate concern "George Borman". Graduated from the Imperial Nicholas Tsarskoye Selo Gymnasium with a silver medal (1915) and Military Medical Academy (1919). Regimental doctor, service in Red Army (1919–24); from the first steps of medical practice sharply felt the need to verify its clinical diagnoses, so he began to make autopsies in unfavorable conditions of Eastern Bukhara, where sectional table served as a door removed from the hinges. Junior, senior lecturer, Department of Pathology, Military Medical Academy (1924–41) and simultaneously Head (1929–63), consultant (1963–67), Pathomorphological Department, Leningrad Cancer Institute with simultaneous work as Head of WHO International Reference Center for Histological Classification of Ovarian Tumors and Head of Department of Pathology, GIDUV named after S.M. Kirov; Chief pathologist of Red Army (1942–44), seriously wounded (1942), demobilized by illness (1945). Corresponding member (1946), academician of the USSR (1960). Research interests: Oncomorphology, infectious pathology and pathology of wartime and other. Author of over 70 scientific works. Distinctive feature: High insistence to himself and to his disciples, adherence to principles. Hobbies: Subtle connoisseur and collector of Russian painting. He died at 71st year of life from a cerebral hemorrhage, not surviving 1 day before his birthday and is buried in Bogoslovsky cemetery of St. Petersburg.
Professor Oleg Konstantinovich Khmelnitsky, Russian pathologist, scientist, and educator (04.11.1920 - 8.02.2004): Born in village Preobrazhenskoe of Luzhskoy district of Petrograd province. Graduated from the 1 Leningrad Medical Institute named after academician I.P.Pavlov (1942). Doctoral thesis on "Pathological anatomy and some questions of pathogenesis of visceral candidiasis" (1963). Military service (1942–45): work in special teams for study of postmortem pathologic anatomy gunshot wound in a combat zone; within 900 days of blockade worked in the besieged city; Head (1963–96), Professor of the Department of Pathology with the course of Cytology, at the same time Chief Scientist, Pathological Laboratory, St. Petersburg Medical Academy of Postgraduate Education (SPMAPE) (1996–04). Chief Pathologist of the Leningrad Department of Health (1965–75). Honored Scientist of the RSFSR (1982). Corresponding Member of the USSR AMS (1986). WHO expert on the histological classification of thyroid tumours. Honorary Doctor of Science SPMAPE with the award of mantle (2000). Research interests: Pathology of mycoses , endocrine, immune, and bone-joint systems, diagnostics of gynecological diseases, philosophical problems of medicine, pathological aspects of geographic pathology. The author of 360 scientific works, including 25 monographs, guidelines and other. He died in St. Petersburg at the age of 83 years and is buried at the cemetery Bolsheokhtinskoye.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-21 Other Topics

PS-21-001
Patella- unusual localisation of bone tumours
J. Jevtic*, R. Kovacevic, Z. Vucinic, G. Djuricic, D. Ristic, J. Sopta
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Objective: Tumours of the patella are very rare. Primary tumours are much more common than metastases. According to literature, the most frequent primary patellar neoplasms are chondroblastoma and giant cell tumour.
Method: A total of 25094 medical records from Register of bone and soft tissue lesions biopsies were included in the study.
Results: Only nine (0.04 %) patients had patellar tumours. Six of these were benign, one was a pseudotumoural lesion and two was reported as malignant. Benign primary bone tumours diagnosed in patella were: two osteochondromas, chondroblastoma, enchondroma, osteoblastoma, cavernous hemangioma. Malignant tumour were: metastasis of urothelial carcinoma and multiple myeloma. Brown tumour in hyperparathyroidism was diagnosed in one case. Eight patients were male, and just patient with hyperparathyroidism was female. The youngest patient was a 9 years old boy with osteochondroma and the oldest was 68 years old male with plasmacytoma. Clinical presentation was unspecific pain and swelling. A patient with solitary metastatic urothelial carcinoma was presented with pathological fracture. Patients were treated surgically, and in two cases (chondroblastoma and metastatic urothelial carcinoma) total patellectomy was performed.
Conclusion: Although very rare, patellar neoplasms should be considered whenever patients complain about symptoms related to knee area. Early diagnosis and adequate treatment insure excellent prognosis.

PS-21-002
Aquaporin 1 and Fibulin-3 as potential biomarkers of malignant mesothelioma in workers occupationally exposed to Fluoro-edenite fibres: A preliminary report
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*AOU Policlinico G. Martino, Dept. of Human Pathology, Messina, Italy

Objective: Aquaporin 1 (AQP1) and Fibulin-3 (Fb-3) have been proposed as biomarkers for the diagnosis and prognosis of malignant pleural mesothelioma (MPM). An increased standardised incidence and mortality rate due to MPM in Biancavilla, a little town of eastern Sicily (Italy) was observed in general population exposed to a natural fiber Fluoro-edenite (FE). The aim of the present study was to investigate the immunohistochemical expression of AQP1 and Fb-3 in a cohort of patients affected by MPM related to FE exposure.
Method: Pathological reports, clinical and follow-up data from eight patients who underwent surgery for MPM, all resident in the town of Biancavilla and exposed to FE. AQP1 and Fb-3 were processed by DAKO Autostainer. AQP1 overexpression was defined when ≥ 50 % of tumour membranous cell staining; Fb-3 immunoexpression was achieved by densitometric and morphometric analyses.
Results: Immunohistochemical overexpression of AQP1 was documented in 5 cases, which showed a significantly higher disease free survival (29.1 months) in comparison to that observed in patients with no AQP1overexpression (7.5 months). In six cases, nuclear and cytoplasmic expressions, of Fb-3 in neoplastic cells were revealed.
Conclusion: Our findings stress the role of AQP1 and Fb-3 in MPM tumourigenesis, with a potential diagnostic and prognostic role.

PS-21-003
Two rare dedifferentiated bone tumours
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Objective: In dedifferentiated osseous neoplasias two distinct constituents can be observed: a low-grade well differentiated sarcoma and a high-grade dedifferentiated sarcoma, the latest dictating the overall prognosis. We present two cases of dedifferentiated bone tumours.
Method: Case 1: a 55 year-old woman with a history of sacrococcygeal chordoma treated with surgery, chemotherapy and radiotherapy, complained of bilateral lumbar pain, paresthesias and hypoesthesias during a follow-up appointment; imaging studies revealed a volumous lesion within the sacrococcygeal region; the patient was re-interventioned. Case 2: a 66 year-old man with a negligible medical background, presented with a femoral pathologic fracture; an intra-medullary lesion was identified intraoperatively.
Results: Case 1: the diagnosis of a dedifferentiated chordoma was established, unfortunately without follow-up information for control since the patient belonged to other institution. Case 2: the surgical specimen heralded a biphasic tumour displaying a well-differentiated chondrosarcoma component and a high-grade sarcomatous component with epithelioid morphology; the clinical management remains to be decided through multidisciplinary consensus.
Conclusion: Chordoma is a rare tumour and its dedifferentiated variant represents an exceedingly rare entity. Dedifferentiated chondrosarcoma is also an uncommon neoplasm which develops only in 10–15 % of the central chondrosarcomas. We report two cases of such entities and a review of the literature.

PS-21-004
Robust and reproducible pathologist training for PD-L1 assessing tumour cells (TC) and immune cells (IC) utilising novel digital training platform
E. Dennis*, B. Vennapusa, E. ElGabry, E. Walker, D. Smith, J. Cardona, M. Kockx
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Objective: PD-L1 expressed on TC and IC plays an important role in down-regulating anti-cancer immune responses and may predict benefit of PD-L1/PD-1 inhibitors. Thus, assessment of TC and IC is incorporated in the VENTANA PD-L1 (SP142) Assay (SP142 Assay) scoring algorithm. IC scoring is a new parameter for companion diagnostics and pathologist training is recommended. Traditional glass slide training covering one specific cut-off is expensive, time-consuming and challenging for broad global reach. An innovative approach was developed to provide a standardized, robust and practical training model.
Method: A universal scoring approach with TC and IC bins for non-small cell lung cancer (NSCLC) and IC bins for urothelial cancer (UC) was developed. A novel digital platform was customized with a rapid, user-friendly interface, facilitating monitoring of scores and reporting. 74 cases, each with three slides (H&E, negative control, SP142 IHC) were uploaded. A global train-the-trainer program enabled local training sessions to be conducted using the digital platform.
Results: 410 pathologists were trained in 29 countries. Average Proficiency Test score was 94 % and pathologist satisfaction score 4.7/5.
Conclusion: SP142 Assay training for TCs and ICs across the dynamic range of staining on a novel digital training platform is robust and successful with excellent pathologist concordance scores.

PS-21-005

Cryoembedder, automatic processor/stainer, liquid nitrogen freezing, and manual staining for frozen section examination: A comparative study

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Objective: Frozen section examination (FSE) can be burdened by several artifacts. We qualitatively analyze a commercial system, composed by a cryoembedder and a processor/stainer, comparing it to our current technique.
Method: Twenty-seven neoplastic specimen were analyzed under the following conditions: Traditional (liquid nitrogen freezing and manual staining), only-Presto (liquid nitrogen freezing and commercial processor/stainer (Presto, Milestone Diagnostic, Italy)), only-PrestoChill (cryoembedder (PrestoCHILL, ibidem) and, manual staining), and PrestoSystem (cryoembedder and processor/stainer). Two pathologists scored feasibility of diagnosis as well as overall architecture, cytology, and staining, using a three-level score (inadequate; satisfactory; excellent). We compared PrestoSystem, Only-PrestoChill and Only-Presto Vs traditional.
Results: Pathologists had substantial agreement on diagnosis feasibility. We observed less variation in scores of PrestoSystem compared to Traditional. Specimens scoring inadequate in diagnosis were all in the frozen in liquid nitrogen groups. PrestoSystem scored equal or better than Traditional, improving the diagnosis score in 45 % of cases; moreover, scores for cytology, staining and architecture were significantly better for PrestoSystem than Traditional. Only-Presto and Only-PrestoChill received better scores for diagnosis than Traditional in 20 and 30 % of cases, respectively.
Conclusion: PrestoSystem was always equal or better in diagnosis compared to traditional technique. The freezing process have been found as the most critical step.

PS-21-006

New materials for bone regeneration based on FastOs®BG and beta-TCP bioglass: Histological evaluation vivo study

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Objective: The evaluation of the efficacy of two biomaterials: FastOs®BG alkaline-free bioactive glass and bioactive glass based composite material and β-TCP doped with 5 ‰ Sr, 1 ‰ Zn and 0.5 ‰ Mn (65β-TCP-FastOs®BG) were applied to head bone defects of Wistar rats.
Method: Two bone defects 3 mm diameter on calvaria of Wistar rats were performed by trepanation and filled with the two biomaterials independently; 9 weeks after, bone regeneration was evaluated: RX and Von Kossa staining.
Results: Bone defects filled with FastOs®BG had higher density than bone defects filled with 65β-TCP-FastOs®BG: 56.5 and 23.2 respectively. Bone density of the defect treated with FastOs®BG was similar to native bone (66). Von Kossa corroborated as FastOs®BG presented 46.95 % while with 65β-TCP-FastOs®BG it was 37.98 % of mean new bone formation respectively.
Conclusion: FastOs®BG bioactive glass promising results as bone graft regeneration needs further scientific support in near future towards β-TCP Sr, Zn and Mn bioglass, to possibly be applied in dental medicine routine.

PS-21-007

Cell block - the bridge between histopathology and cytology

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Objective: The widespread use of liquid-based cytology rises the possibility of preparing cell blocks from the fluid used for the detection and diagnosis of lesions, both in gynecological and in non-gynecological samples. The aim of our study was to present the advantages and disadvantages of using cell blocks in cytology for diagnostic purpose.
Method: In this study, we selected cases in which patients were known with neoplastic lesions or not, in order to investigate the diagnostic value and validity of examining cell block slides and to determine the effectiveness of this method by comparing the cell block cytomorphology and immunhistochemical stain versus conventional cytology, in both gynecological and non-gynecological preparates.
Results: A total of 46 samples were collected for this study. From these a number of 26 were gynecological samples and the remaining 20 samples consisted of ascites fluid, pleural fluid and fine needle aspiration from the breast. The samples were processed by performing a conventional smear and by making a cell block, and results were evaluated.
Conclusion: The combined use of conventional cytology and cell block increase remarkably accurate cytologic diagnosis. In suspected lesions, cell block is a superior technique than smear by establishing a classification of the lesion. Cell block offers increased cellularity compared to conventional cytology. Multiple sections can be obtained for special stains and immunohistochemical study, with applications in the differential diagnosis. Therefore, along with the conventional cytology, cell block can be used as an adjuvant in evaluating fluid aspirates in order to obtain a final diagnosis as accurately as possible.

PS-21-008

Optimised in vitro model for testing the molecular background of tumour damage caused by modulated electro-hyperthermia

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Objective: By inducing heat shock at ~42 °C, modulated electro-hyperthermia (mEHT) can selectively damage malignant tumours. For rapidly testing molecular changes we set up an in vitro tumour model and optimized mEHT treatment conditions.
Method: Confluent coverslip cultures of C26 mouse colorectal adenocarcinoma cell line were treated with mEHT at 42 °C for 2 × 60 min, 60 + 30 min, 2 × 30 min or for 30 min, respectively leaving 120 min intervals between interventions. After 24 h, stress response, apoptosis and growth signaling related markers were detected compared to untreated control cultures.
Results: Tumour damage rate of ~50 % (LD50) was achieved after 2 × 30 min mEHT treatment, while other combinations killed the majority of tumour cells. Significant translocation of phosphatidyl-serine to the outer cell surface detected with annexin V flow cytometry indicated massive apoptosis. Elevated levels of heat stress induced Hsp70 and calreticulin, as well as cleaved caspase-3 and cytoplasmic phospho-ERK1/2 proteins were also revealed in situ.
Conclusion: Our results indicate that molecular changes related to cell stress, apoptosis and growth regulation upon mEHT treatment in C26 colorectal carcinoma cultures can be best analyzed after 2 × 30 min interventions. Repeated, as opposed to single intervention, better simulate human mEHT treatment used complementary either to radio- or chemotherapy.

PS-21-009

Challenges of problem based learning in teaching pathology

R. Baral*
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Objective: Patan Academy of Health Sciences (PAHS) was established in 2008 with aims to produce physicians who would be able and willing

to serve in the rural areas. This is the only medical institution in Nepal which has adopted the Problem Based Learning (PBL) in undergraduate teaching. The aim of this study is to do a critical analysis of PBL in teaching Pathology and evaluation of undergraduate students.
Method: Review of entry criteria and curriculum along with observed need in teaching and evaluation.
Results: Competency based training as a part of adult learning is the strength; and the weakness is inadequate information of the pathogenesis of diseases to the students, lack of timely clarification of confusions and ineffective guidance during PBL sessions. There is systematic communication gap between student, teacher and guardian to analyze the progress of the student.
Conclusion: There is no match between students expectations and teachers guidance to deliver appropriate knowledge and skill for future physician. Students are engaged in teaching and learning activities for a quarter of academic hours only. Neither teachers nor guardians know the progress report of individual student.

PS-21-010
Growth pathway inhibition, apoptosis and immune response caused by modulated electro-hyperthermia in colorectal cancer allografts
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Objective: Non-invasive modulated electro-hyperthermia (mEHT) can induce selective heat shock (at 42oC) and damage in cancer. Earlier we showed mEHT provoking significant apoptosis inducing factor (AIF) mediated cell death and immune cell infiltration in HT29 colorectal cancer xenografts of immunocompromised mice. In this study, we tested mEHT related damage responses using tumours grown in immunocompetent mice.
Method: C26 colorectal cancer allografts (CRCA) were treated for 30 min using single shot mEHT. The expression of heat shock, growth-, damage signaling and immune response associated proteins was tested in situ and in vitro.
Results: Loco-regional mEHT treatment caused significant caspase-dependent apoptosis in C26 CRCA with reduced phospho-Raf 1; and elevated phospho-ERK1/2 protein levels of dominantly cytoplasmic localisation. Ki67 protein expression disappeared completely from mEHT affected tumour cell nuclei. mEHT promoted the release of damage-associated molecular pattern (DAMP) proteins such as Hsp70, calreticulin and HMGB1. In line with this, the number of tumour infiltrating S100+ antigen-presenting dendritic cells and CD3+ T-cells showed major increase.
Conclusion: In immunocompetent mice, mEHT treatment interfered both with cell cycle progression and the MAP kinase related downstream growth pathway. Increased expression and translocation of phospho-EKR1/2 might contribute to caspase dependent apoptosis, which induced DAMP signalling and elevated immune response in C26 CRCA.

PS-21-011
Molecular and ethnic analysis of non-cutaneous melanoma in Singapore
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Objective: Determination of ethnic ratios for all melanoma. Within the non-cutaneous group to further analyse molecular data for ckit and BRAF mutations and compare with Western figures.
Method: Cases of melanoma were retrieved from SGH files over 8 years, 2009–2017, and a subset subjected to molecular analysis for BRAF and ckit. The samples were analysed for mutations in exon 15 of the BRAF gene, and exons 9, 11,13, and 17 of the ckit gene in genomic DNA by polymerase chain reaction amplification and and direct Sanger sequencing.
Results: Acral and mucosal subtypes each constituted approximately 32 % of the population, and cutaneous represented 35 %. Each category majority were Chinese, highest being in the acral (86 %) and mucosal (76 %) categories. A total 37 cases of non-cutaneous melanoma underwent molecular analysis,majority being Chinese (76 %). Extracting highest number subsets yielded results as follows; Head and neck: ckit 0/6, BRAF 2/11; GIT: ckit 3/7, BRAF 0/7 Gynaecologic: ckit 1/9, BRAF 0/9
Conclusion: Of all cases of melanoma, a high percentage of acral and mucosal types are seen in the Singapore population. In this Chinese majority ethnic population molecular analysis of noncutaneous melanoma demonstrates a higher ckit + ve rate (18 %), and lower BRAF rate (7 %) in comparison with cutaneous melanoma, and similar to Caucasian ethnic group.

PS-21-012
Correlations between tumour metabolic profiles and tumour destruction induced by modulated electro-hyperthermia
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Objective: Elevated glycolysis (Warburg effect), lactate and ion concentration in cancer can contribute to selective tumour destruction by modulated electro-hyperthermia (mEHT) at ~42oC. In this study we correlated mEHT treatment efficiency and the glycolytic profile in 3 tumour cell lines.
Method: Levels of glycolytic enzymes, metabolits of glycolysis and oxidative phosphorylation, as well as buffer pH and buffer capacity were tested in mouse (C26) and human colorectal carcinoma (HT29) and in human hepatocellular carcinoma (HepG2) cell cultures. These cell lines were also grown in mice and treated with mEHT.
Results: Intracytoplasmic lactate levels measured using mass spectrometry were 58 % higher in C26 than in HT29, and 37 % higher than in HepG2 cells. Citrate levels were 119 % higher in C26 than in HepG2, while only 32 % higher than in HT29 cells. Buffer capacity showed an inverse correlation, HepG2 > HT29 > C26, suggesting the most acidic environment also in C26 cells. In line with this, in vivo tumour destruction ratio 24 h after treatment showed also a similar correlation HT29 ≥ C26 > HepG2. Immunohistochemistry demonstrated high glycolytic enzyme levels, without significant difference between cell lines.
Conclusion: Glycolytic profile, particularly elevated acidification and ion concentration supports the accumulation of electric field in tumours and the efficiency of mEHT treatment.

PS-21-013
Autofluorescence imaging is useful for the detection of lymph node metastases in unstained paraffin sections
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Objective: Fluorescence lifetime imaging (FLIM) is a light microscopic technique providing additional information on tissue molecules. The method is based on the time delay ("lifetime") between the excitation of molecules and the emission of the fluorescence photons. which depends on the molecule structure and the physico-chemical environment. A virtual fluorescence lifetime image is created by transforming lifetime values in pseudo-colors for each pixel. For theoretical reasons, this technique should be able to recognize metastatic cells inside lymphatic tissue.
Method: We collected from the files 25 cases of routinely formalin-fixed and paraffin-embedded lymph nodes containing carcinoma metastases..

FLIM images of unstained slides of dewaxed histologic sections were obtained by a confocal microscope equipped with a pulsed laser at 405 nm, and a time-correlated single-photon counter.
Results: Whereas lymphatic tissue showed only very weak or no autofluorescence signals, metastatic carcinoma cells revealed usually prominent cytoplasmatic autofluorescence, thus permitting easily their detection on screening. In neuroendcrine neoplasias, the cytoplasmic autofluorescence showed dot-like features. Furthermore, mucin production was easily recognizable because of its strong FLIM signals with short life times.
Conclusion: Due to striking differences between the autofluorescence characteristics of lymphatic tissues and many cancer metastases, the FLIM technique may be helpful for the detetction of lymph node metastases.

PS-21-014
Microfluidics for rapid cytokeratin immunohistochemical staining in frozen sections
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Objective: Develop a complete pan-cytokeratin chromogenic staining protocol that could be performed in intraoperative conditions using a microfluidic tissue processor (MTP).
Method: Anonymized frozen samples from ureter, pancreas, prostate, breast carcinoma, pancreas adenocarcinoma, lung adenocarcinoma (NSCLC) and Hodgkin lymphoma were used. Sections were dried using cold air for 2 min, fixed for 3 min in cold acetone and dried again using cold air for 2 min. All the subsequent steps of the staining were performed on the MTP-device, including anti-cytokeratin primary antibody (AE1/AE3), secondary antibody, DAB and counterstaining.
Results: Our microfluidic technology delivered fast (<12 min) and automated IHC stains using conventional anti-cytokeratin antibodies on multiple frozen tissue types. Results showed specificity to cells of epithelial origin and low levels of background in the negative controls. The performance of the protocol was controlled against manual assays.
Conclusion: Since the increased time performance relies on the microfluidic handling and not on the reagents themselves, our technique has the potential to provide pathologists with a versatile tool for fast IHC stainings on frozen sections of any type. We believe that many more questions could be answered intraoperatively with the use of our new technology to reduce the turn-around time of IHC assays.

PS-21-016
Tissue preservation, aliquoting methods and quality controls in biobanking
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Objective: CRO-Biobank (CRO Aviano NCI, Italy) is a structured facility integrated in a clinical setting aimed at collecting human biological samples for cancear research. Our mission is to organize a collection of OCT-embedded frozen (−80 °C) and FFPE tissue samples with paired biomaterials (e.g. serum, plasma, buffy coat, and nucleic acids). We are testing different histological fixatives, alternative to formalin (which is toxic and carcinogenic) finalized to clinical diagnosis, molecular analysis and biobanking of PE tissues.
Method: We use well-de_ned methods to control tissue quality: histocytology (frozen sections, FFPE mirrored samples and cytological imprints) and molecular analyses. We randomly perform molecular assays based on DNA, RNA and protein extracts.
Results: Based on the model of "Expert Centers", a specific activity of tumour biological characterization has been planned in our Institution, using aliquots stored in our biobank. NGS, proteomic and immunohistochemical preliminary analyses will provide highly informative biosamples to the researchers. We elaborated an "aliquoting system" that allows to select the appropriate quantity of material delivered for a single project and may warrant appropriate selection of cells for research purposes.
Conclusion: We are implementing quality processes to guarantee the operator's safety, the patient's privacy, and the traceability and quality of samples.

PS-21-017
Development of an annotated ontology-driven whole slide image library of normal and abnormal human tissue
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Objective: This work describes the process and outcome of a pilot project to build a large and comprehensive database of annotated whole slide images (WSI) of normal and abnormal human tissue, and to link the annotations to appropriate ontological information.
Method: WSI of normal and abnormal tissue from 51 colon resections and 8 skin excisions, diagnosed 2015–2016 at the Linköping Department of Clinical Pathology, were randomly collected. These images were manually annotated at the level of major sub compartments, including normal or abnormal findings and artifacts. If abnormal the abnormality was specified. SNOMED-CT was chosen as the most suitable ontology after a literature review, and the annotations were linked to its codes and terms.
Results: 117 WSI, 136 levels, were collected and annotated from colon and skin, resulting in 3005 annotations, covering a total area of 106.4 gigapixels (266 cm2). 49 unique SNOMED-CT codes were used. The time taken to annotate a WSI varied from 45 s to over 120 min.
Conclusion: Images and annotations from WSI were successfully gathered and linked to SNOMED-CT codes. Annotating images is time consuming, the development of better annotation tools will be helpful. This work has informed future plans to build a comprehensive library of images.

PS-21-018
Deferral and discordance rates of intraoperative consultations in different organ systems
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Objective: The pathologists' interpretation in intraoperative consultations is either definitive or defers the final diagnosis to the permanent sections. This study investigates the deferral and discordant rates in different organ systems.
Method: The intraoperative decisions (diagnosis vs. deferral) on 1096 surgical pathology cases (excluding neuropathology) were compared to the final diagnoses. The discordance and deferral rates were determined in the different organ systems and the findings were analyzed.
Results: The overall discordant rate was 2.9 %. Thyroid cases represented only 1.4 % of all cases, but they had the highest discordant rate (15 %), followed by head and neck (4 %), gastrointestinal (4 %) and lymph node cases (3.1 %). 67 % of the discordances were due to sampling error, the remaining 33 % were due to diagnostic misinterpretations. The overall deferral rate was 11.5 %. Soft tissue cases showed the highest deferral rate (30.9 %), followed by gynecologic (21.9 %) and lung cases (21.5 %).

Conclusion: In most discordant cases the difference in the intraoperative and final interpretations is due to sampling and not interpretative errors. Cases where ancillary studies or extensive sampling is necessary to make the final diagnosis show the highest deferral rates.

PS-21-019

Discordance rates in different types of intraoperative consultations

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Objective: Intraoperative consultations are sent for different reasons and handled by different methods depending on the clinical question and the pathologists' preferences. We investigated the discordant rates between the intraoperative and the final diagnostic interpretations on cases sent for diagnostic interpretation vs. margin check, and cases diagnosed by frozen section vs touch imprint.
Method: Intraoperative interpretations were compared to the final diagnoses on permanent paraffin sections. The discordance rate was determined for diagnostic interpretations (1042) vs. margin checks (293), and frozen sections (1142) vs. touch imprints (81). Cases sent for gross examination only, for both diagnosis and margin check or handled by both frozen section and touch imprint were excluded.
Results: The discordant rate was higher for margin checks (3.75 %) than for diagnostic interpretations (2.11 %). Cases handled by frozen section had a lower discordant rate (2.54 %) than touch imprints (3.7 %). Cases handled by frozen section and accompanied by a smear were excluded from the comparison, however they showed the lowest discordant rate (0.94 %).
Conclusion: Intraoperative consultations for margin involvement have a higher discordant rate than diagnostic interpretations. Touch imprints have higher discordant rates than frozen sections, while cases frozen section is combined with smears show the lowest discordant rate.

PS-21-020

Discordant rates between intraoperative and final diagnostic interpretations of cases with documented consultations

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Objective: Getting a consultation on challenging cases is an encouraged practice to deliver appropriate quality assurance in surgical pathology. Pathologists often make diagnostic interpretations under time pressure during intraoperative consultations to determine the next step in patient care. We have compared the discordant rates between the intraoperative and the final diagnostic interpretations on cases where documented consultation was obtained to cases where it was not.
Method: 1349 intraoperative consultations were reviewed at the laboratories of Diagnostic Services Manitoba. Intraoperative interpretations on frozen sections and touch imprints were compared to the final diagnostic interpretations on permanent paraffin section diagnoses. The rate of discordance on cases with a consultation was compared to the cases where no consultation was documented.
Results: The overall discordant rate was 2.52 %. Documented consultation was recorded in 6.3 % of all cases. Within this group the discordant rate was significantly higher than in the group where documented consultation was not recorded (5.9 % vs. 2.3 %, $p < 0.05$).
Conclusion: The results may be explained by the fact that the more straightforward cases are signed out with no consultation. Cases with documented consultation likely represent a particularly challenging subset of cases, where the discordant rate would be even higher without consultations.

PS-21-021

Preterm labor: Histophatological findings

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Objective: Preterm labor (PTL) delivery occurring before 37 completed weeks, comphehends 11 % of deliveries and 70 % of all perinatal mortality.
Method: A series of 24 PTL with rigorous criteria and a control group - healthy singleton pregnancy without pre-existing diseases, were monitorized in Obstetric routine: first prenatal appointment before the 14th week; gestation between 24 weeks + 0 days and 33 weeks + 6 days; intact amniotic membranes; cervical length_25mm; use of atosiban (competitive antagonist of oxytocin receptors) for tocolysis, were common the main criteria.
Results: Placentas full thickness tissue samples/sections of approximately 0.2 and 0.5 cm3 were formalin-fixed paraffin-embedded. Histophatological registration of chorionic plaque, upper and lower halves of placental tissue and decidua characteristics was accomplished.
Conclusion: Beyond subchorionic fibrin plaque/Langhans' fibrinoid thickeness and partially hyalinized deciduas, PTL placentas had endothelial hyperplasia emerged as a selective feature of immature placentas, exhibited mainly in chorionic/stem villi vessel endothelial cells (predominantly in arteries). This lesion had not been described before to the best of our knowledge.

PS-21-022

Histopathologic challenges in diagnosing the spectrum of diseases in the axilla: An analysis of axillary masses in a tertiary hospital of a developing country

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Objective: to determine and analysis the spectrum of diseases that are commonly encountered in the axilla and the challenges the histopathologic differential diagnoses of the various categories the pathology
Method: Ten years consecutive axillary biopsy specimens sent to the pathology laboratory were formalin fixed, paraffin embedded and stained with Haematoxylin and Eosin. Stains such as Ziehl Neelsen, vermentin and CDs 5, 20, 23 were also employed in further differentiation of diseases. Data analyzed using SPSS Version 16.0
Results: Fifty nine axillary lesions were analysed from 21 males and 38 females. The ages ranged from 2 months to 80 years and peaked in the 3rd decade of life. There were eight developmental (congenital) lesions (13.6 %), seven infectious (12.0 %), 12 reactive (20.3 %) and 31 neoplastic lesions (52.5 %). All the congenital lesions were aberrant breast tissues. There were 19 non neoplastic lymph nodes and 12 of them (63.2 %) were reactive hyperplasia remaining (35 %) being granulomatous inflammations of which four were tuberculous. The neoplastic diseases were dominated by lipoma; 5 cases (16.1 %), non Hodgkin's lymphoma; 11cases (35.5 %), and metastatic carcinoma; 5 cases (16.1 %).
Conclusion: The most common tissue of affectation in the axilla was the lymph node. Malignant neoplastic diseases were the commonest with a female predisposition the peaked in third decade of life.

PS-21-023

A comparative study of formalin, ethanol, jaggery and mepivacaine in tissue fixative efficacy

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Objective: Formalin is a gold standard for tissue preservation. However, formalin poses several health hazards. Identification of non-toxic, readily available fixative agent is necessary. The objective of this study was to compare tissue fixative property of three agents, including 30 % jaggery, 70 % ethanol and 2 % mepivacaine with epinephrine 1: 100,000 to 10 % formalin.
Method: 24 pieces of soft tissue received from standard oral surgical operation were included. The tissue was sectioned into 0.5 x 0.5 x 0.3 cm. Each piece was fixed in four different fixatives, 6 pieces for each group, for 24 and 72 hrs at room temperature. All tissue were then fixed in 10 % formalin for another 24 hrs and processed according to standard protocol. The cellular structure and outline and staining quality of H&E-stained sections were scored from one to three by pathologist, who was blinded from the experimental groups. Average fixative efficacy score among the four groups were analyzed by Kruskal-Wallis.
Results: No significant difference was found between 70 % ethanol, 30 % jaggery and 10 % formalin at both 24 and 72 hrs. However, mepivacaine showed statistically significant lower fixative efficacy than the other three groups.
Conclusion: Seventy percent ethanol and 30 % jaggery maybe used as transport fixative agent and alternatives to formalin.

PS-21-024
The prognostic significance of cancer-associated fibroblasts in pancreatic ductal adenocarcinoma
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Objective: Cancer-associated fibroblasts(CAF) are abundant in the desmoplastic stroma of pancreatic ductal adenocarcinomas(PDAC), and are considered to play important roles in tumour progression. We investigated the expression status of secreted protein acidic and rich in cysteine(SPARC), periostin(POSTN), fibroblast-activated protein(FAP) and proCOL11A1 antibody in the stroma of PDACs and their prognostic implications.
Method: Tissue microarrays were constructed from 155 surgically resected PDACs and paired non-neoplastic pancreata, and from independent set of 48 normal/benign pancreata, and immunohistochemical stains were performed for proCOL11A1, FAP, SPARC and POSTN. The immunohistochemical stains results were correlated with clinicopathological features and survival data.
Results: Four antibodies' expression was significantly increased in the intratumoural stroma of PDACs compared to paired non-neoplastic pancreata (proCOL11A1: 145/155(93.5 %) vs 26/154(16.9 %); FAP: 139/143(97.2 %) vs 82/132(62.1 %); SPARC: 113/150(75.3 %) vs 49/132(37.1 %); POSTN: 135/151(89.4 %) vs 45/135(33.3 %); $p < 0.001$, all). There were no significant differences in the expression frequencies among normal pancreas, acute and chronic pancreatitis. On survival analysis, low FAP-positive intratumoural CAF counts (<100/HPF) was associated with a significantly reduced overall survival compared to those with high FAP-positive CAF counts($p = 0.010$; hazard ratio 5.2(95 % confidence interval 1.3–21.3)).
Conclusion: We demonstrate that the presence of peritumoural CAFs may not always be associated with a poor prognosis as suggested in many studies; it may be supporting the recent experimental findings that tumour stroma may have a protective role rather than enhance aggressive behavior.

PS-21-025
Prevalence of ßIII-tubulin (TUBB3) expression in human normal tissues and cancers
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Objective: Microtubules are involved in crucial cellular roles. Class-III-ß-tubulin (TUBB3) is a microtubule protein, expressed in cells of neuronal origin and various tumour types. TUBB3 is of clinical relevance as overexpression has been linked to poor response to microtubule-targeting anti-cancer drugs such as taxanes.
Method: To systematically investigate the epidemiology of TUBB3 expression in normal and neoplastic tissues we used tissue microarrays (TMAs) for analyzing the immunohistochemically detectable expression of TUBB3 in 3911 tissue samples from 100 different tumour categories and 76 different normal tissue types.
Results: At least one tumour with weak expression could be found in 93 of 100 (93 %) different tumour types and all these 93 entities had also at least one tumour with strong positivity. In normal tissues, a particularly strong expression was found in neurons, endothelium, fibroblasts, spermatogenic cells and endocrine cells. In tumours, strong TUBB3 expression was most frequently found in various brain tumours, malignant melanomas and lung cancer, pancreatic adenocarcinomas and renal cell carcinoma.
Conclusion: In summary, these results identify a broad spectrum of cancers that can at least sporadically express TUBB3. Testing of TUBB3 in cancer types eligible for taxane-based therapies could be helpful to identify patients who might best benefit from this treatment.

PS-21-026
High-throughput tissue microarray: The utility of high-density pile-up array
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Objective: One of the few high-throughput tissue microarray methods is the cutting edge matrix assembly method. Its manufacturing method is complicated. Therefore, we developed a novel high-density pile-up array by improving the high-throughput tissue microarray. With this technique, 240–500 tissue cores can be analyzed simultaneously.
Method: Retrospectively, 414 formalin-fixed and paraffin-embedded surgical specimens from 140 lung cancer cases were used. A high-density pile-up array was prepared from 160 to 250-μm-thick formalin-fixed and paraffin-embedded sections that were laminated into horizontal sections using a hollow needle. Sections containing only paraffin were used as spacers between tissue cores.
Results: The tissue core loss rate using the high-density tissue microarray was approximately 10–30 % (range, 145–540 tissue cores) while using 0.6-mm-diameter tissue cores. In the high-density pile-up array, it was 0–10 % while using 160-200-μm-prism tissue cores. These findings demonstrated that high-density pile-up array was superior to high-density-tissue microarray due to a lower rate of tissue cores loss. High-density pile-up array is composed of tissue material and paraffin and can thus be easily tailored to specific tissue core sizes and inter-core spacing.
Conclusion: The high-density pile-up array method can efficiently make tissue microarray in general facilities.

PS-21-028
The borderland of embryology and pathology revisited: Two cases of tailgut cysts
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Objective: Tailgut cyst is a rare presacral lesion, most likely deriving from remnants of the post-anal part of the primitive gut ("tailgut"). Though congenital, it usually manifests in adults. We herewith report two cases.

Method: A 29-year-old female (case A) and a 62-year-old male (case B) both presented with lower intestinal symptoms. Imaging disclosed presacral lesions. Specimen A consisted of a 7 x 4.6 cm opened cystic wall; a 6.5 cm large fragment containing a 3.4 cm unilocular cyst filled with yellowish thin fluid, together with the coccyx, were received in case B.
Results: Both cysts were lined with non-keratinising squamous epithelium. Moreover, specimen A presented extensive ulceration with xanthogranulomatous inflammation and granulation tissue; whereas, in specimen B areas covered by columnar, non-ciliated epithelium containing mucus cells, as well as bundles of smooth muscle fibres were seen. Lack of structured intestinal wall excluded an enterogenous duplication cyst, absence of neural elements a neurenteric duct cyst, whereas absence of other tissues excluded a presacral teratoma. No malignancy was documented in either specimen.
Conclusion: Embryologic malformations should always be included in the differential diagnosis of lesions in this area.

PS-21-030
A 13-year-old female with hemolacria and hemoptysis
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Objective: Background Hematidrosis is an exceptionally rare disease that was associated with religious beliefs, high blood pressure, menses, stress and systemic disease. However, pathophysiology and etiology are still largely unknown.
Method: A complete medical and family history was obtained, physical examination and a detailed laboratory were conducted. A spectrum of autoimmune and oncological diseases were assayed. Ultrasounds, radiography, echocardiography, endoscopy, esophago-gastro-duodenoscopy were performed for final diagnosis.
Results: The patient's past medical history was unremarkable. Physical examination was unexceptional for any abnormal findings. All of the labs were reported to be within normal limits. All of the assays for autoimmune diseases were negative. Bronchoscopy and gastroduodenal endoscopy were normal. The patient was discharged without diagnosis. After repeated bleedings a hematologist diagnosed this patient with hematidrosis.
Conclusion: Here we report a case of a 13-year-old girl who frequently bled from the scalp, eyes and ears. Investigation at multiple facilities by paediatric nephrologists, hematologist-oncologists, immunologists, psychiatrists, and endocrinologists provided no diagnosis. The diagnosis is consistent with this patient as she seemed to exhibit issues when she was stressed and her blood pressure increased.

PS-21-031
Contribution to predict Oncotype DX recurrence score from pathologic features in luminal B breast carcinoma using artificial neural networks
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Objective: Oncotype DX (ODX), genomic test ,predict a recurrence score(RS) of breast cancer at 10 years and estimate chemotherapyefficiency. Artificial Neural Networks(ANN) are mathematical modelsfor classification and predictiontasks. The ame is to Use artificial networks to predict the ODXRSfrom histological and immunohistochemical features in luminal B breast carcinoma.
Method: Retrospective study (2012–2016)50 patients,paraffin-embedded tumour tissue: HES stain, immunohistochemistry (estrogen receptor (ER), progesterone receptor(PR) ,HER2, ki67),molecular analysis(Genomic Health Inc). ANN trained to prognosis the ODXRS, 3classes ANN/ 3ODXRS levels, 10 tests combinations (age, size, node, grade SBR, differentiation, atypia , mitosis count ,ER , PR , ki67) .
Results: ComparaisonRS withANN to ODXRS : concordance 41 % with all the input attributes , (62.5 %) without age,tumour s' size , lymph node status (15/24 well classified tumours). 9 tumours misclassified in 50 % of the tests .intermediateTumoursodxrs /lowrisk ANN . 7 tumours well classified in 70 % of the tests: tumours with low and high risk always well classified.
Conclusion: The results prove that ANN can predict correctly RS in 62 % of the cases. Others workswith increasing cases are necessary.

PS-21-032
Peritoneal malignant mesothelioma, deciduoid pattern in a young patient: A case report
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Objective: Malignant mesothelioma (MM) involving the peritoneal cavity is a rare disease with about 1 case per 4–5 million of the population worldwide. There is a lesser male predominance as with pleural manifestation. Asbestos exposure is one of the main causes accounting for 60 % of peritoneal tumours.
Method: Two peritoneal tissue samples of a 27 year old male were excised and consecutively examined histomorphologically. To distinguish between primary and secondary lesions, we used various immunohistochemical markers.
Results: The infiltrative growth pattern as well as the epithelioid character of the tumour cells in context with various positive immunohistochemical markers such as MNF-116, Calretinin, Vimentin, led to the diagnosis of a malignant epithelioid mesothelioma. Because the tumour cells closely resembled that of the decidua, the features were consistent with a deciduoid subtype.
Conclusion: Although rare, MM has been described in younger patients even without knowledge of a prior exposure to asbestos. The deciduoid subtype of this tumour can be diagnostically challenging, especially in women. The prognosis is poor with a median survival of 12 months.

PS-21-033
Umbilical metastasis as a primary manifestation of cancer with unknown origin: Report of two cases
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Objective: Umbilical metastasis can be the first manifestation of an undiagnosed malignant disease. It represents the first sign of a primary malignancy or a metastatic site of an already diagnosed cancer, representing an ominous prognostic finding.
Method: We report the case of a 45-years-old-woman and a 59-years-old-woman, who both presented with umbilical hernia. During surgery, a firm nodule 2 cm and 1,7 cm respectively, was found.
Results: Histological examination revealed an adenocarcinoma infiltrating the dermis and subcutaneous tissue. Immunohistochemical examination showed a cytokeratin 7 positivity while it was negative for ER/PR receptors, TTF-1, WT-1, Calretinin and GCDFP-15. Furthermore, the first case showed a weak staining for ER receptors and the second, for cytokeratin 20, CDX2 and CEA, in a small percentage of neoplastic cells. Further diagnostic evaluation included upper and lower gastrointestinal-tract endoscopies, abdominal and thoracic MRI. Consequently, the first patient was diagnosed with ovarian endometrioid carcinoma and the second patient with high-grade gastric adenocarcinoma of intestinal type.

Conclusion: In conclusion, umbilical metastasis is an uncommon manifestation of visceral malignancies, related to an advanced disease. Therefore, careful evaluation, including an early biopsy, of all umbilical lesions is recommended and immunohistochemistry is of great value for determining their primary origin.

PS-21-034

Primary pleural primitive neuro-ectodermal tumour: A rare entity

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Objective: Primary neuro-ectodermal tumours (PNETs) are rare and highly malignant. Pleural involvement is exceptional. The aim of this study is to describe its clinico-pathologic features.
Method: We reported an exceptional case of a pleural PNET.
Results: A 51-year-old man presented with chest pain, cough and dyspnea. Chest computed tomography revealed a pleural compressive mass with necrosis areas. CT guided biopsy of the mass was performed. Histological examination revealed an undifferentiated round cells tumour. The tumour cells were positive for CD99, NSE, pancytokeratin, synaptophysin and vimentin. Based on these histologic and immunohistochemical findings, the diagnosis of pleural PNET was made. The extension assessment was negative and the patient was recieved chemotherapy. Radical pleuro-pneumonectomy, enlarged with pericardium and diaphragm with mediastinal lymph node dissection was performed. The histological examination of the surgical specimen showed the presence of the same tumour infiltrating the pericardium, the diaphragm and the pulmonary parenchyma. Operative follow-up was favorable.
Conclusion: Pleural PNET are exceptional, highly malignant and very aggressive. They should be considered in the differential diagnosis of thoracic tumours regardless of the age of the patient.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-22 Pathology in Favour of Developing Countries

PS-22-002

High preponderance of BRAF V600E mutation in papillary thyroid carcinoma (PTC) among Filipinos: A clinicopathologic study

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Objective: BRAF mutation in papillary thyroid carcinomas (PTC) is associated with an aggressive phenotype, with an incidence of 45 %. We evaluated the prevalence of BRAF mutations in PTC in Filipino patients, and correlated with clinicopathologic characteristics.
Method: From June 2016 to December 2016, clinic-pathologic data were retrieved from 64 patients who underwent total thyroidectomy. Tumour DNA was isolated using the QIAmp FFPE extraction kit. BRAF exon 15 was amplified using the following primers: F-TGCTTGCTCTGATAGGA, R-GGCCAAAAATTTAA TCAGTGG and sequenced with the ABI3500 Genetic Analyzer.
Results: 18/64 (28 %) were diagnosed as PTC. 12 out 17 (70.6 %) PTC cases harbored BRAF V600E mutation, 1 case failed to amplify. Demographics of patients with PTC included 13 females, 5 males, median age of 46 years old (range 25–74). 14 cases showed conventional subtype, 2 follicular variant, 1 oncocytic variant, and 1 with tall cell features. The average tumour size was 3.01 cm (range 0.8–7 cm), extrathyroidal extension was 7/18 (38.9 %), multifocality 6/18 (33.3 %), and lymph node involvement 8/18 (44.4 %). All parameters did not predict BRAF mutation.
Conclusion: Given its associated prognostic value, the high preponderance of BRAF mutation (70.6 %) suggest some correlation with previously reported lower 5 year survival among Filipinos. This warrants further investigation in a larger cohort.

PS-22-004

Prevalence and factors associated with vitamin D deficiency among Afghan adolescents

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Objective: this study aimed to determine the prevalence and identify factors associated with vitaminD deficiency and severe vitaminD deficiency among Afghan adolescents (10–18 years) diagnosed at French Medical Institute for Mothers and Children
Method: An analytical cross-sectional study design was conducted from Jun to Sep 2016. Blood samples were obtained, serum 25OHD levels were measured, and the patients were divided into five diagnostic categories according to their serum 25OHD concentrations. Sufficiency ≥ 30–100 ng/ml; Insufficiency 20–30 ng/ml; Deficiency < 20 ng/ml; Severe deficiency < 10 ng/ml; Intoxication >150 ng/ml. Collection of samples were made at Clinical Laboratory of FMIC and serum 25OHD analyses were carried out in the Biochemistry section
Results: A total of 308 adolescents were part of the sample for the final analysis. Of all, 202(65.6 %) were females and 106(34.5 %) were males. Out of total, 238(77.3 %) had either insufficiency, deficiency or severe deficiency of vitaminD. Among those, a large number of the participantss 107(34.7 %) had severe vitaminD deficiency, 81(26.3 %) had vitaminD deficiency, 50(16.2 %) had vitaminD insufficiency, and only 70(22.7 %) had vitaminD sufficiency. There were two cases of vitaminD intoxication, who were excluded from the study. Gender, sun-exposure, usage of sun protector, calcium + vitaminD supplement intake, VitaminD rich foods intake, regular milk intake, the type of living in yards or apartments, skin colour of participants, and BMI were found as significant factors associated with vitaminD levels
Conclusion: Low serum vitaminD concentration is prevalent among general Afghan population. Screening and ongoing investigation for vitaminD deficiency should be considered for all adolescents in the country

PS-22-008

Odontogenic cyst: An epidemiologic study with histopathological review

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Objective: Odontogenic cyst represent a diverse group of pathologic lesions of the jaws. The current classification of the odontogenic cyst has two main categories of cyst: developmental and inflammatory. In this study were reviewed in retrospect all the cystic lesion of the jaws diagnosed at City Hospital Of Timisoara over a period of 5 years.
Method: All the jaw specimens that had a clinical diagnosis of cystic mass that were received during our study period were included. The clinicopathological data were retreived from the records. The slides were reevaluated, classified and disscussed.
Results: We found 185 inflammatory and developmental jaw cysts. The most common lesions were inflammatory with cases of perapical cysts (n = 161) and residual cysts (n = 7) followed by developmental cyst with cases of dentigerous cysts (n = 14) and odontogenic keratocysts (n = 3). There was a male predominance (n = 97,

8–84 age range). The body of the mandible was the commonest site (n = 131), followed by the maxilla (n = 54, mostly in the alveolar process region).
Conclusion: Diagnosis of jaw cysts requires the integration of clinical and pathological findings. This study showed that the majority of the odontogenic cystic mass of the jaws are inflammatory.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-23 Soft Tissue and Bone Pathology

PS-23-001
Immunohistochemical analysis of a series of rhabdomyosarcomas diagnosed at a Tertiary Cancer Referral Centre
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Objective: To evaluate immunohistochemical features of a series of 300 rhabdomyosarcomas (RMSs).
Method: Immunohistochemical expression of myogenin and MyoD1 was graded, based on percentage of tumour cells displaying positive intranuclear immunostaining, namely grade 1 (1–25 %); grade 2 (26–50 %); grade 3 (51–76 %) and grade 4 (76–100 %).Outcomes/ follow-up details were available in 272 (90.7 %) patients. High myoD1 and myogenin immunoexpression (in more than, equal to 51 % tumour cell nuclei) were correlated with various subtypes.
Results: There were 140cases (46.7 %) of alveolar RMS(ARMS), 90 of embryonal RMS(30 %), 61(20.3 %) of spindle cell/ sclerosing RMS and 9cases(3 %) of pleomorphic RMS. Immunohistochemically, desmin was expressed in 292/299(97.6 %) tumours, myogenin in 238/267(89.1 %), MyoD1 in 192/266(72.2 %), synaptophysin in 17/71(23.9 %), S100 protein in 11/75(11.5 %), WT1 in 18/29(62 %) and variable MIC2/CD99 in 61/148(41.2 %) tumours. High myogenin expression was significantly associated with cases of ARMSs (95/121,78.5 %), compared to other subtypes(48/117, 41 %)($p < 0.001$). High MyoD1 expression was seen in more cases of pure sclerosing and spindle cell/ sclerosing RMSs (10/10, 100 %), compared to the other subtypes (91/141, 67.4 %)($p = 0.032$).
Conclusion: This study reinforces significant association between high myogenin expression and cases of ARMS, as compared to other subtypes. High MyoD1 expression was seen more in cases of spindle cell/sclerosing RMSs. Certain RMSs, especially ARMS also display neuroendocrine differentiation.

PS-23-002
Desmoid type fibromatosis: Clinicopathologic analysis of 113 cases
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Objective: Recurrence relation with surgical margin status, tumour location and patient age were evaluated in desmoid type fibromatosis with current follow-up.
Method: Patients diagnosed as desmoid type fibromatosis between 2000 and 2016 were evaluated.
Results: Of these 113 cases, 42 were male and 71 were female, median age was 33 ± 18 (4–95). Twenty two (19 %) of them were younger than 17 years old. Of these cases 74 (66 %) were extraabdominal, 24 (21 %) were abdominal and 15 (13 %) were intraabdominal. Extraabdominal tumours were mostly located at lower extremity (%47). Of the 54 follow-up known cases, recurrence occurred in 18 cases (33 %). Of these 18 cases, 6 were younger than 17 years old. Of these 18 cases extraabdominal, abdominal and intraabdominal locations were 16, 1 and 1 respectively and the relation between tumour location and recurrence was significant (p = 0,031) . Of the 90 cases whose surgical margin was evaluated, 81 % were positive. Significant correlation was found between surgical margin status and recurrence (p = 0,023). There was no recurrence in 16 cases whose the surgical margins were positive (median follow up 59 months). Sixty four tumour were studied immunohistochemically with Beta catenin and nuclear positivitiy was seen in 53 tumour (83 %).
Conclusion: Desmoid type fibromatosis is a locally agressive tumour. Extraabdominal location and positive surgical margin status are risk factors for recurrence. Some tumours may stable for some years though margin positivity.

PS-23-003
Review of pleomorphic liposarcomas in La Paz Hospital
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Objective: Our aim was to review all the pleomorphic liposarcomas and dedifferentiated liposarcomas with pleomorphic components (considered separately due to differences in prognosis) diagnosed in La Paz In the period 1965–2017.
Method: We searched our database for all liposarcomas and selected the pleomorphic liposarcomas and dedifferentiated liposarcomas with pleomorphic features diagnosed in our centre and retrieved clinical data about sex, age and location.
Results: Among the 291 liposarcomas diagnosed in our centre we found 20 cases of pleomorphic liposarcoma and dedifferentiated liposarcoma with a pleomorphic component. The mean age was 58 years (range 32–88) and the distribution was similar among sexes (55%F/45%M). The most common location was the leg (60 %), followed by the retroperitoneum (10 %) and the chest wall (10 %). Most of the tumours were predominantly composed of a high grade sarcoma (pleomorphic undifferentiated sarcoma-like), with the diagnostic pleomorphic lipoblasts being a minoritary component.
Conclusion: Pleomorphic liposarcoma is a rare entity, and the most uncommon subtype of liposarcoma. We submit the experience from our centre for over more than 50 years in order to help to define and understand better this infrequent tumour. The scarcity of the diagnostic areas emphasizes the necessity of an extensive sampling in order to avoid underdiagnosing.

PS-23-004
Case report: Secondary osteosarcoma arising in the femur of a 26-year-old woman with a long-standing benign orthopaedic condition
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Objective: Osteosarcoma arising in association with metallic orthopaedic devices(DCS) in benign conditions (symple bone cyst-SBC) is rare, understudied and has unknown mechanisms. Our pacient known with SBC had multiple surgical orthopaedic interventions for complications (infection, fracture) and ultimately developed an osteosarcoma.
Method: We present a case of a 26-year-old woman with a long history of disease. Thirteen years ago the patient suffered a pathologic fracture of the right femoral neck due to SBC, underwent orthopaedic reduction and plaster cast immobilization, healed with secondary coxa vara, limb shortening and difficulty walking. In 2010, was admitted for open curettage

with bone grafting, Pauwels osteotomy and plate osteosynthesis using DCS with favorable recovery. At that time, histopathology was negative for malignancy and the radiologic data supported the findings. The patient was stationary on routine radiologic examination(available-end 2013). In 2017, presented with pain/difficulty walking, radiology showed the presence of the osteosynthetic metallic material and changes indicative of malignancy, no metastasis. Arteriography with right AFP embolisation and surgical biopsy were done, followed by segmental femoral resection with modular bipolar prosthesis, good recovery. The surgical specimens were adequately processed-histopathologically/immunohistochemically examined.

Results: On microscopy, histopathological profile was:conventional osteosarcoma with extension in surrounding soft tissue. Immunohistochemic profile: CD56 difusely positive, MDM2-focally positive, S100-positive, Ki67-positive in 40 % of neoplastic cells.

Conclusion: Although very rare, published cases of osteosarcoma secondary to metallic implants do exist. Such cases should be reported because the literature does not provide sufficient data and further studies are needed in assesing additional risk factors, such as infection and trauma.

PS-23-005

New approach to understanding of appearance and progression of osteoarthrosis

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Objective: To study the structural features of the cartilage and the tidemark under osteoarthrosis, to determine the function of the tidemark while the destruction of osteocartilaginous tissue.

Method: We used the following methods: histological and electron-microscopic methods were used for studying the structural features of normal articular cartilage and articular cartilage under osteoarthrosis; immunohistochemical study of p53, osteopontin, osteonectin, type I collagen, type II collagen and MMP1 receptors.

Results: Articular cartilage is represented by two clearly delineated zones (noncalcified and calcified cartilage) that have different histochemical and electron microscopic structural features of parenchymal and stromal components, the tidemark is the boundary between them. Under osteoarthrosis it has qualitative (changes in hematoxylin staining intensity, Van Gieson's staining, PAS reaction, p53, OPN receptors) and quantitative (thickening, dublication, fragmentation and even total disappearance) transformations. This is followed by changes in the structure of articular cartilage and subchondral bone.

Conclusion: Under osteoarthrosis the articular cartilage in accompanied by progressive destruction of extracellular matrix and dystrophic changes of chondrocytes. It is connected with preceding modification of the tidemark that on the one hand serves as the barrier between osteolytic properties of synovial fluid and subchondral bone, and on the other hand—between osteosynthetic stimuli of the bony tissue.

PS-23-006

A case of fatal phosphaturic mesenchymal tumour

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Objective: Phosphaturic mesenchymal tumour (PMT) is a rare neoplasm; the biologic behavior of PMT is currently under investigation. We present a case of PMT with a protracted course over 12 years leading to a fatal outcome.

Method: A 39 year-old man presented with weakness in 2004 and was found to have decreased serum phosphorus, phosphaturia and lack of 1, 25-dihydroxyvitamin D3. Four years later he developed a painful left calf mass. The lesion was resected, but recurred causing extreme pain and dysfunction. Above-knee amputation was performed.

Results: Dissection of the specimen showed multiple soft tissue tumours in all muscle compartments of the calf, measuring up to 18 cm. An additional, separate lesion was found in the distal tibial metaphysis. Histological examination of all lesions showed a cellular spindle cell neoplasm with variously sized vessels, wide vessel-like spaces and scattered deposits of calcified extracellular material. The tumour infiltrated skeletal muscles, subcutaneous fat and the proximal end of the fibula. The tibial lesion had identical histology. Three years after the amputation the patient developed multiple metastases in both lungs and died.

Conclusion: This case illustrates that PMT may not only disseminate locally but also metastasize and cause death.

PS-23-008

Cell cycle regulatory protein expression in multinucleated giant cells: Do they proliferate?

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Objective: By studying replication activity in the mononuclear cell fraction of giant cell tumour of bone (GCTB) we detected cell cycle regulatory proteins also in multinucleated giant cells. Our objective was to test if osteoclast-like giant cells can enter and progress into the cell cycle.

Method: Formalin-fixed, paraffin-embedded sections from 30 GCTB cases were analyzed for the expression of nuclear proteins involved in driving or controling phases of cell cycle progression.

Results: In giant cells, of Ki67 protein specific antibodies, SP6 stained most cell nuclei, while B56 and Mib1; and the replication licensing mcm2 stained occasionally a few. Many nuclei were positive for the cyclin dependent kinase (cdk) 4/6 and all nuclei were stained for its complexing partner cyclin D1. Of later G1/S-phase promoters, cdk2 was rare, while its compexing partner cyclin E, their cdk inhibitor p21waf1, the tumour suppressor p53 and the cell cycle controling cyclin G1 were seen in most giant cell nuclei. However, none of the post-G1 phase markers including cyclin A, geminin or aurora B were noticed in giant cells.

Conclusion: Multinucleated osteoclast-like giant cells show early signs of cell replication which, however, is arrested at late G1-phase possibly driven by p53 induced p21waf1 and cyclin G1 upregulation.

PS-23-009

Coexisting cutaneous Kaposi sarcoma with Leishmania

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Objective: Infection with Leishmania spp is common in HIV (+) patients residing in endemic areas. We herewith describe a rare case of coexistence of Kaposi sarcoma (KS) and leishmaniosis in the same cutaneous lesion in a HIV (+) patient.

Method: A 43-year old HIV (+) patient presented with fever of unknown origin, as well as several violet-colored, elevated, nodular lesions and plaques on the neck, forehead and both hands. A cutaneous punch biopsy was performed, with the working diagnosis of KS

Results: Histology showed typical appearance of KS; neoplastic endothelial cells were immunopositive for HHV-8. Moreover, the lesion abounded with macrophages containing intracytoplasmic, dot- or ring-like inclusions, of a bluish-purple appearance with a Giemsa stain; coexistent leishmaniosis was hinted and confirmed by means of a polymerase

chain reaction detection of Leishmania spp DNA, in paraffin sections from the block.
Conclusion: This case represents an atypical, unusual histological finding and illustrates the need to exclude coexistent infectious diseases in a biopsy specimen of Kaposi sarcoma in an immunocompromised patient

PS-23-010
Malignant transformation of plexiform neurofibroma: A rare case report
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Objective: Malignant peripheral nerve sheath tumour (MPNST) can result from a malignant transformation of benign lesions associated with neurofibromatosis type 1 (NF1), including plexiform neurofibroma (PN).
Method: A 33-year old male patient presented with a mass in the chest. He underwent surgical resection and two irregularly shaped tumour fragments (6 cm and 4.5 cm in diameter) were excised. Histologically, we recognized a spindle cell tumour with myxoid and multinodular areas. Immunohistochemically, the tumour cells were positive for S100, and Vimentin. Contrary, Desmin, CD34, and CD31 were negative. Therefore, the diagnosis of a PN was made. Six months later, the patient showed again a 1.5 cm large tumour at the same localisation. Tumour resection was performed again. Microscopically, the tumour contained spindle cells arranged in a herringbone pattern. Mitotic count was 60/10 HPF, but no necrosis were found. Immunohistochemically, tumour cells were positive for Vimentin, focally for Bcl-2, and few cells showed positivity for CD56, and CD31. S100, SMA, Desmin, CD117, CD34, CD68, EMA, and CK7 were negative.
Results: Finally, the diagnosis of a MPNST was made.
Conclusion: Diagnosis of PN is important. Malignant transformation of a PN in a MPNST can occur, especially in NF1 patients, and therefore patients need close follow-up.

PS-23-011
IgG4-related disease among patients previously diagnosed with idiopathic retroperitoneal fibrosis. A nationwide Danish study
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Objective: To estimate the occurrence of IgG4-related retroperitoneal fibrosis (RPF) in Danish patients diagnosed with idiopathic RPF (IRPF).
Method: The National Danish Pathology Register was searched for patients diagnosed with RPF from 2004 through 2013. Among 724 candidate cases 43 patients were analyzed. Histopathologic features suggesting an IgG4-related disease (IgG4-RD) background were recorded. Cut-off levels for IgG4 positive cells at ≥ 30 per HPF and IgG4: total IgG ratio at ≥ 40 % were applied. Patients were categorized as IRPF, definite or possible IgG4-RD.
Results: Forty three patients were included. 19 (44 %) met the criteria for IgG4-RD comprising 7 with definite, 12 with possible IgG4-RD and 24 with IRPF. Patients with an IgG4: total IgG ratio ≥ 40 % had significantly more histopathologic features of IgG4-RD compared to a ratio < 40 %. Patients with ≥ 30 IgG4+ cells per HPF had higher numbers of eosinophils than those with lower IgG4+ cell counts.
Conclusion: A total of 44 % of IRPF patients was diagnosed with IgG4-RD, 16 % with definite and 28 % with possible IgG4-RD. The closer association of IgG4: total IgG ratio ≥ 40 vs. lower ratios with histopathologic findings supports a direct pathogenic role by IgG4 bearing cells or IgG4 in IgG4 RPF.

PS-23-012
Clinicopathological features of recurrent retroperitoneal liposarcomas: 38 cases
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Objective: The aim of study is determine the relation between clinicopathological features of primary and recurrent retroperitoneal liposarcomas (RLS).
Method: A retrospective review (2009–2016) of clinical, KT, MRI dates, pathohistological and ICH-stainings of recurrent RLS from 38 patients was carried. The number of recurrences varies from 1 to 9: 1 (8), 2(10), 3(5), 4(3), 5(3), ≥6 in 9 cases. Mean age at diagnosis was 58 years (from 36 to 75); male -14, female – 24.
Results: In 40 primary RLS were: 9 myxoid (6 well-differentiated, 3 high-grade round cell); 16 well-differentiated LS (WDLS): lipoma-like -4, sclerosing – 3, inflammatory -2, with myxoid component – 7); pleomorphic RLS -8; dedifferentiated LS– 4. 18 RLS recurred as the same WD and myxoid LS. In 2 cases WDLS with myxoid component recurred as lipoma-like RLS. There is no significant tendency for transformation into dedifferentiated LS (9 cases). Primary WDLS recurred as pleomorphic LS in 8 cases. Dedifferentiated RLS recurred as WDLS in 2 cases.
Conclusion: Variable of histologic patterns in recurrent RLS are common and in cases with multiple nodes varies from lipoma-like histology to pleomorphic LS. The rate for transformation WDLS into dedifferentiated or pleomorphic LS is higher in cases with 4 or more recurrences.

PS-23-013
An osteosarcoma animal model response to photodynamic therapy in combination with doxorubicin
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Objective: Evaluate the outcome of photodynamic therapy (PDT) combined with doxorubicin in an orthotopic animal model of osteosarcoma.
Method: 20 Balb/c nu/nu nude mice were injected in the skull with 2 × 106 cells. They were divided into 4 groups: Group I-6 animals not submitted to therapy; Group II-6 animals treated with PDT based in the photosensitizer(PS)5,15-bis(2-bromo-3-hydroxyfenil)porphyrin, synthesized by us,(2 mg/kg)when tumour reached 200 mm3of volume;Group-III-4 animals treated with a non-therapeutic dose of doxorubicin(2 mg/kg);and Group IV-4 animals submitted to the combination of PDT and doxorubicin. Seventy-two hours after the injection of the PS, animals from Group-II and Group-IV were irradiated. Twelve days later the tumour was excised and the histological analysis was performed.
Results: In Group-I and III we observed a solid round tumour that continues growing. However, Group-II showed a decreased tumour volume when compared to I and III. Regarding the Group-IV, tumour volume was the lowest. It reveals a malignant, very aggressive and necrotic tumour,(33–55 %)which infiltrates and destroys the cranial bone invading the brain space including medulla. Dystrophic calcifications and neoplastic anastomosing bone trabeculae were observed. Small vessels embolism suggest metastasis.The Ki-67 shows a diminish cell proliferation(58 %)when compared to the Group-I(80 %).
Conclusion: The combination seems to have a better outcome and deserve further studies.

PS-23-014

Lymphoid aggregates in tissue around revised hip and knee replacements - implant based differences

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Objective: For adverse biological reactions with perivascular lymphoid aggregates (PLA) in tissue around failed metal-on-metal (M-O-M) joint prostheses, special name »aseptic lymphocyte-dominated vasculitis associated lesion (ALVAL) « has been proposed. Our aim was to characterise histologically and immunohistochemically PLA in a large series of periprosthetic tissue.
Method: We retrospectively analysed histological slides from 1069 patients obtained at the revision arthroplasties. Cases with PLA 2+ or 3+ according to Oxford-ALVAL scoring system (severe PLA with lymphocyte cuffing more than five cells in thickness) were included in the study.
Results: We found PLA in 53 (4.9 %) cases: 27 (3.8 %) from hip and 26 (7.1 %) from knee revision arthroplasties. According to Oxford-ALVAL scoring system 31 cases were 2+ and 22 cases were 3+. In one hip case primary prosthesis was M-O-M, in five ceramic-on-ceramic and in one case ceramic-on polyethylene. In the remaining 20 hip cases and in all 26 knee cases metal-on-polyethylene bearing couples were revised. CD3+ lymphocytes were found in most cases. No correlation between Oxford-ALVAL scoring system and other histological and immunohistochemical characteristics of periprosthetic tissue were found.
Conclusion: PLA are not specific for M-O-M joint prostheses, therefore each case with PLA has to be considered separately to determine the cause of such histological picture.

PS-23-015

Paratesticular fibrous pseudotumour: A new entity of IgG4-related disease?

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Objective: Paratesticular fibrous pseudotumour represents (PFP) a benign tumour-like lesion confined to intrascrotal, paratesticular areas. Due to the rarity of the lesion, both pathogenesis and clinical management are little understood Recently, it has been postulated to be among the spectrum of immunoglobulin G4-related diseases.
Method: We describe a case of PFP from a 41 year-old man presented with a slowly-growing, painless right intrascrotal mass over the last 3 years clinically favored malignant mesothelioma. A magnetic resonance imaging scan revealed a diffuse-proliferated nodular mass at the paratesticular area with very low signal density on T2-weighted imaging.
Results: Grossly, nodular tumour with testicular compression was noted without intra-testicular infiltration. Histologically the lesion consisted of collagen-rich hyalinized fibrotic tissue with storiform patterns. There were scattered lymphoid tissues and phlebitis was also noted. The immunoglobulin G4 staining showed infiltration of positive plasma cells with highest count 52 per high-power field, whereas the mixed Kappa and Lambda immunoglobulin light chain expression indicated the polyclonality of the plasma cell population. Following local excision, the patient has been well for 2 years.
Conclusion: The specific histological and immunohistochemical features documented in our case support to the theory of PFP being IgG4RD which usually occur in young adulthood and can mimic testicular malignancy clinically. Typical radiological, morphological and immunohistochemical features may help to separate this lesion from malignant tumours which may save the patients from aggressive surgical interventions.

PS-23-016

Hybrid low grade fibromyxoid sarcoma-sclerosing epithelioid fibrosarcoma of the kidney: An unusual case with EWSR1-CREB3L1 fusion

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Objective: Low-grade fibromyxoid sarcoma (LGFMS) and sclerosing epithelioid fibrosarcoma (SEF) are uncommon tumours with distinct sets of morphological features, both characterized by MUC4 immunoreactivity. Tumours exhibiting features of both entities are considered hybrid LGFMS-SEF lesions. The majority of LGFMS cases are characterised by FUS-CREB3L2 gene fusions, with few cases showing FUS-CREB3L1 and EWSR1-CREB3L1 gene fusions. In contrast, the majority of pure SEF cases show EWSR1 gene rearrangements, with rare cases showing FUS gene arrangements. In the largest study of hybrid LGFMS-SEF tumours to date, all cases exhibited FUS and CREB3L2 rearrangements, a similar genetic profile to LGFMS.
Method: We herein report an unusual case of hybrid LFMS-SEF occurring in a 10 year old child with a primary renal tumour and disseminated metastases.
Results: Histology of the primary renal tumour showed a spindle cell neoplasm with features of a LGFMS. In contrast, histology of a cervical lymph node metastasis showed cords of epithelioid cells in a sclerotic stroma, characteristic of SEF. Genetic characterization of the separate LGFMS and SEF components revealed an EWSR1-CREB3L1 gene fusion in both.
Conclusion: To our knowledge, this is the first reported case of a hybrid LGFMS-SEF occurring in the kidney. This case also provides further evidence that a subset of hybrid LGFMS-SEF harbour EWSR1-CREB3L1 gene fusions. In this case, these features were associated with an aggressive clinical course, with disease associated mortality occurring within 12 months of diagnosis.

PS-23-017

Intimal sarcoma: A case report

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Objective: Intimal sarcomas are malignant tumour with first described in 1923 by Moritz Mandelstamm, with a greater prevalence in the middle aged and females. Only approximately 210 cases had been described.
Method: Here, we report two cases intimal sarcoma of splenic and pulmonary arteries
Results: Case one: A 72 y.o.- female with a 5 kg weight loss over the past 1 years, abdominal pain, nausea, vomiting. Imaging demonstrated a 41x30mm solid, heterogeneously enhancing tumour of the tail of the pancreas with invasion to splenic artery. The patient underwent a laparoscopic distal pancreatectomy with splenectomy. Gross a white to gray tumour that measured 4.0 cm with the invasion of the splenic artery. Histologically the tumour was comprised of spindled cells in a fascicular growth pattern with cigar-shaped nuclei, intracytoplasmic vacuoles, and exhibited marked nuclear pleomorphism. Mitotic figures were numerous and necrosis was present. Case two: A 55-y.o.-female with diagnoses mixoma right atrium. Gross a white to gray tumour that measured 5.0 cm. Histologically the tumour was comprised of spindled cells in a fascicular growth pattern with cigar-shaped nuclei and exhibited nuclear pleomorphism. Mitotic 5/50 HPF. IHC tumour cells both cases stained diffusely positive for vimentin, moderately intense staining for SMA and the CD34. Given the histologic features and IHC this tumours was classified as an intimal sarcoma. The first case intimal sarcoma of the splenic artery; the second case pulmonary artery intimal sarcoma with extension to the right atrium. ICD-O 9137/3.

Conclusion: due to the aggressive nature of intimal sarcoma, rapid recognition is needed in order to decrease the time between diagnosis and treatment.

PS-23-018

Unusual histology of metastatic desmoplastic small round cell tumour in lung: Way to pitfall

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Objective: Desmoplastic small round cell tumour (DSRCT) is a rare and aggressive malignant neoplasm that occurs mainly in abdomen and pelvis. About 40 % of patients have metastatic disease to the lungs, liver, spleen, or bones at diagnosis. Wide range of morphologic appearances of DSRCT creates diagnostic challenges.
Method: We present a case of metastatic DSRCT with unusual histology that led to incorrect diagnosis without complete clinical information.
Results: A 55-year-old female presented with incidental mass at left upper lobe, founded on fluorography in May 2014, which subsequently was resected. Well circumscribed, firm tumour was found. Microscopically, the neoplasm is composed of small, round to oval cells, generally uniform in size and shape. Cells were closely packed in solid mass, without any interfering stroma. Immunohistochemical study revealed expression of AE1/3 (focal), Vimentin, CD99, Bcl-2, SMA; while S100, CD34, Synaptophysin and TLE were negative. The diagnosis of sarcomatoid carcinoma was proposed. At the same time 5 cm nodule was found on ultrasound investigation in plane of left ovary, initially interpreted as benign. One year later enlarged pelvic mass was removed. The histopathological features in the form of island, nests and trabecules of monomorphic small round to ovoid cells dispersed within a prominent fibroblastic stroma as well as polyimmunophenotypic profile were characteristic of DSRCT. Molecular study, which have identified a specific EWSR1 translocation in both samples supports the diagnosis of DRSCT with metastasis to the lung.
Conclusion: Careful clinicomorphological investigation of the patient is crucial for the correct recognition of the rare entity and subsequent adequate therapy.

PS-23-019

Malignant TFE3-rearranged perivascular epithelioid cell neoplasm (PEComa) in the masticator space in a child

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Objective: PEComas are rare mesenchymal tumours composed of epithelioid and/or spindle cells with a myomelanocytic immunophenotype. A subset of PEComas harbours translocations involving the transcription factor gene TFE3. Malignant criteria proposed by Folpe et al. include tumour size, infiltrative growth, nuclear grade, cellularity, necrosis, vascular invasion and mitotic rate as important prognostic factors.
Method: Case report: A 7-year-old boy with a bulging mass in the left masticator space. The MRI shows a polilobulated solid mass of 4,7 cm with defined borders and necrotic center, that pushes the adyacent structures in the soft tissues.
Results: The neoplasm grows in expansive lobules composed of uniform discohesive clear cells, distributed in nests and cords, with 3 mitosis per 50 high power fields, microscopic necrosis and tumoural vascular invasion. The immunoprofile is positive for nuclear TFE3, HMB45, focal Melan-A, and smooth muscle actin. FISH for TFE3 gene rearrangment is positive.
Conclusion: The differential diagnosis of tumours with clear cell features and/or (myo)melanocytic differentiation includes alveolar sarcoma, clear cell sarcoma and PEComa without TFE3 rearrangment. There are very few cases with the characteristics shown here reported in the literature.

PS-23-020

Diagnostic utility and limitation of immunohistochemistry and dual color in situ hybridisation for the diagnosis of dedifferentiated liposarcoma

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Objective: To analyze the utility and limitation of immunohistochemistry and dual color in situ hybridization (DISH) for the diagnosis of dedifferentiated liposarcoma (DDLPS) lacking obvious lipogenic components.
Method: Materials contained ten cases of DDLPS and 17 cases of non-lipogenic, high-grade sarcomas. All DDLPSs lacked clear-cut lipogenic differentiation in the specimens analyzed. Immunohistochemical analyses were performed for p16, CDK4, and MDM2. The amplification of MDM2 gene was investigated with DISH.
Results: All DDLPSs were immunoreactive for p16, CDK4, and MDM2. Positive cells were more than 50 % in most specimens. DISH analyses also exhibited high-level amplification of MDM2 gene in all DDLPSs. On the other hand, among non-lipogenic sarcomas, p16, CDK4, and MDM2 were expressed in eight, nine, and three cases, respectively. The MDM2 gene amplification was detected in three of eight studied. With the careful reevaluation of these three sarcomas, two were reclassified as DDLPS, as small areas of lipogenic components could be detected in other specimens.
Conclusion: The present study confirmed the utility of immunohistochemistry for MDM2 expression and DISH for MDM2 gene amplification in the diagnosis of DDLPS, especially when lipogenic components were obscure for some reasons. Furthermore, DISH seems to be more practical than FISH.

PS-23-022

Fibro-osseous pseudotumour of the digits

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Objective: Fibro-osseous pseudotumour of the digits (FOPD) is an uncommon soft tissue lesion that may be mistaken for malignancy. The aim of our study is to present an illustrative typical case report to avoid inappropriate treatment of this benign entity.
Method: We report the case of a 60-year-old manual worker male who presented with a localised fusiform painless mass involving the left thumb. Conventional radiography demonstrated an ill-defined soft tissue mass with focal calcification, while MRI revealed cortical erosion and adhesion to the adjacent flexor tendon. Surgical biopsy confirmed the diagnosis of FOPD and therefore complete local excision was performed.
Results: FOPD is a benign rare ossifying lesion that predominates in the upper extremity of young females. Repetitive small mechanical injuries are recognized to be a predisposing factor. Clinical and imaging features are not specific. Histologically, the tumour shows typically a non-zonal biphasic fibo-osseous proliferation involving the subcutis. The main pathologic differential diagnoses are myositis ossificans, and extraskeletal osteosarcoma as mitoses may be numerous. Finally, prognosis is excellent if the tumour is totally removed.
Conclusion: Diagnosis of FOPD requires precision as it should be differentiated from myositis ossificans, and extra-skeletal osteosarcoma. Local recurrence is unusual and malignant transformation is very rare.

PS-23-023

Paediatric Perivascular Epithelioid cell tumour (PEComa): A case report and a review of the literature

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Objective: Perivascular Epithelioid Cell tumours (PEComas) are a rare group of mesenchymal tumours composed of distinctive cells originating from blood vessel walls and express melanocytic and smooth-muscle markers (HMB-45, AML). This tumour family occurs typically in females (F:M = 6/1) with a peak incidence at 45 years of age and includes angiomyiolipoma, lymphangioleiomyomatosis, clear cell sugar tumour, and tumours arising in various visceral and soft tissue sites. PEComas of paediatric age are rare with less than 40 cases being described, mainly in patients older than 5 year-old.
Method: We will report a case of a 10-year-old female black patient, with asymptomatic vesicular lithiasis, presenting with a painless abdominal mass, found incidentally during a routine abdominal ultrasound.
Results: A mass was located in the periumbilical region, with predominantly solid mixed characteristics. Further evaluation was followed by MRI and Angio-CT, which revealed a well-limited intraperitoneal mass compressing the inferior vena cava and molding to anterior abdominal wall as it was not possible to define any type of vascular invasion.
Conclusion: Although most cases are benign, few malignant cases have been reported. The morphological and immunohistochemical aspects were compatible with the diagnosis of PEComa. Given the size of the lesion (>5 cm), its classification was of uncertain malignant potential.

PS-23-024

Congenital (infantile) fibrosarcoma of the scalp: A case report

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Objective: Infantile fibrosarcoma (IFS) is a relatively rare tumour in newborn, infants and small children. There is a male predominance. The principal sites of involvement are the extremities, the next most common sites of involvement are the trunk, head and neck. But scalp involment is exeptionally rare.
Method: A 3-year-old Syrian girl presented with an occipital ekstracranial mass. At radiologic examination the tumour was located in the right occipitoparietal region and was subcutenous.
Results: The mass was 335 g and sized 9x9x8cm. Cut surface was gray-white, necrotic and hemoragic. On microscopic examination, the tumour composed of sheets of solidly packed spindle-shaped cells that are arranged in bundles or fascicles, imparting a herringbone appearence. The cells show little nuclear pleomorphism and are mitotically active. The tumour cells were immunoreactive for vimentin and focally for SMA but were negative for myogenin, desmin, CD34. The result of histologic study revealed infantile fibrosarcoma.
Conclusion: IFS of the scalp is rare and have a good prognosis. Despite histopathological similarities, IFS behave very differently to their adult counterpart. Congenital IFS has lower metastatic potential and better outcome as compared with fibrosarcomas occurring in adults. We are presenting this case because of its rarity.

PS-23-025

Kaposi sarcoma of rectosigmoid: A rare case report

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Objective: Kaposi sarcoma is a vascular neoplasm that has large age range with a slight male predominance, affecting more often AIDS patients with HHV8 infection. KS appears mainly in the skin, while visceral organs, such as rectum and sigmoid, are less frequently affected. We describe a rare case of KS in a 77y.o. man arising in the rectosigmoid.
Method: Our patient presented with a mass in the left colon and rectosigmoeidectomy was performed. The surgical specimen was formalin –fixed and processed for histopathological and immumohistochemical study.
Results: Gross examination revealed numerous ulcerated reddish brown polypoid lesions , sized 0,4 cm to 2,6 cm. Histology showed multiple lesions composed of spindle cells separated by slit-like vessels, extravasated red blood cells, hemosiderin laden macrophages, lymphocytes and fibrosis with invasion of muscularis propria, pericolorectal tissues and all the regional lymph nodes. Immunohistochemically, the tumour cells stained strongly for HHV8, CD34, CD31 and focally FVIII.
Conclusion: Colorectal KS can mimic other vascular or mesenchymal tumours such as angiosarcoma, fibrosarcoma, GIST, melanoma etc. We should carefully examine the specimen and co-assess patient's clinical and laboratory status, as involvement of colon by KS is rare, with only few published case reports.

PS-23-026

Angiomyofibroblastoma presenting as an inguinal hernia in a male patient: A case report

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Objective: To report a rare case of benign myofibroblastic tumour presenting as inguinal hernia.
Method: A 62 year-old male was hospitalized with a slow growing, painless, inguinal mass. It was considered an inguinal hernia and surgical intervention was performed. The well defined mass was sent for histologic examination.
Results: On cut section, an encapsulated nodule of 50 mm in diameter was identified, without necrotic areas. This was microscopically composed of elongated cells with edged or round margins and infrequent large nuclei, without atypical mitoses. Some of these cells showed multivacuolated cytoplasm. The stroma was well-vascularized and presented focal myxoid features. The tumour cells displayed positivity for desmin, CD34, estrogen and progesteron receptors and were negative for smooth muscle actin (SMA), Ki67 and S100. Based on the clinicopathological features and immunoprofile, the final diagnosis was angiomyofibroblastoma. The differential diagnosis took into account the cellular angiofibroma and aggressive angiomyxoma.
Conclusion: Although angiomyofibroblastoma is a benign tumour, differential diagnosis with an aggressive angiomyxoma should be attentively perform, for a proper follow-up. These tumours can be pure or show overlapping features.

PS-23-027

Chondromyxoid fibroma: Report of three cases

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Objective: Chondromyxoid fibroma is a benign neoplasm. Generally, it occurs in the metaphysis of a long bone and has benign radiographic appearance.
Method: Case 1: A 70 years old woman with long history of left knee pain. Case 2: A 42 years old man with a several months history of right leg pain. Case 3: A 71 years old man with history of right arm pain. In almost all three cases XR showed a lobulated, eccentric radiolucent lesion geographic bone destruction, well defined sclerotic margin, presence of

septations (pseudotrabeculation), presence of matrix calcification in small proportion.
Results: The pathology showed in two of the cases a lobulated pattern, although this growth pattern may be absent as we sow on the second case. The xamples contain bone and the edges of the tumour are rounder and retract from surrounding bone. The lobules consist of spindel and stellate cells embedded in a myxoid background. The cells have abundant pink cytoplasm, producing epithelioid appearance.
Conclusion: Chondromyxoid fibroma is a rare neoplasm. Some reports have suggested a male predominance. Patients range in age from 3 to 87 years. Approximately 45percent of the lesions occur in the long bones. The main differential diagnosis is chondrosarcoma.

PS-23-028
Soft tissue perineurioma: A case report
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Objective: Perineuriomas are rare nerve sheath tumours composed of well-differantiated perineural cells that have a distinct ultrastructural and immunohistochemical phenotpe. Two variants are recognized: intraneural perineuriomas and soft tissue perineurioma. Most of these neoplasm are benign, but perineuriomas of low-grade malignant potential and malignant form have also been reported. Soft tissue perineurioma clinically manifest as a painless nodule occurs mostly in superficial soft tissue, an only infrequently affects deep soft tissue of the extremities or trunk.
Method: A 41-year -old woman presented with a palpabl mass in the right forearm. The mass was excised.
Results: Grossly, the tumour measured 0.9x0.6x0.5 cm. The cut surface was pale gray and rubbery soft. Histological examination showed that the tumour was composed of spindle cells within myxoid stroma. The tumour cells elongated, tapering nuclei and were arranged in fasciculer, whorled pattern. The tumour cells were positive for epithelial membrane antigen and negative for S-100 protein.
Conclusion: We present a case of extraneural (soft tissue) perineurioma highlighting clinical, pathologic and immunohistochemical features along with a discussion of the main differential diagnosis of this tumour.

PS-23-029
Alveolar soft-part sarcoma (ASPS) of the m. triceps surae - case report
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Objective: Alveolar soft-part sarcoma (ASPS) is a rare malignant soft tissue tumour. It typically arises in the extremities. ASPS has a specific der(17)t(X;17)(p11.2;q25) translocation. Other sarcoma specific molecular markers usually are negative.
Method: Here we present case of ASPS in 10 years old boy. Tumour was found in m. triceps surae.
Results: Tumour consisted nests of tumour cells, separated by sinusoidal vascular channels. They formed lobules of different sizes, divided by dense fibrous septs. Cells were discohesive. The cells were large polygonal and less pleomorphic, with distinct cell borders and vesicular nuclei, containing nucleoli and abundant granular cytoplasm. Mitotic figures were rare. Immunohistochemically tumour cells were negative for sarcoma and epithelioid markers (EMA -, AE1/AE3 -, 34b/E12 –, Desmin–, Vimentin –, aSMA-, CD56 -, S100 -, Synaptophysin–, CD34 -, CD99 –, GFAP –, Ki67 - 6 %). Only TFE3 were positive in tumour cell nuclei and FISH method showed break in TFE3 gene (These analyses was done in reference laboratory: Institute of Pathology, University of Kiel, Germany).
Conclusion: ASPS is rare diagnosis, especially in small countries. It is not always possible to perform all necessary diagnostic tests. Differential diagnosis manly mainly based on histology and exclusion of other soft tissue tumours.

PS-23-030
Clear cell sarcoma of the hand: Mimicking a palm phlegmon in a young adult
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Objective: To worn clinicians about a rare sarcoma entity that may mimic an infection
Method: case report
Results: A 66 years old man with no family history of neoplasia, and no other pathological personal history but being a smoker of 100 pack-years of cigarettes, who works as a manual labor has consulted with 4 cm swelling of the left hand's palm associated to local inflammatory signs without any impact on the patient's general physical condition. Initial diagnosis was phlegmon of the left hand's thenar area, and it was processed by excision and double intra-venous antibiotic but the local state was aggravated therefore re-excision was resumed in addressing the material for pathologic analysis which revealed the diagnosis of clear cell sarcoma of the left hand. An MRI of the left hand as well as a chest TDM and an abdominal ultrasound were made. And in the face of the very fast worsening of the left hand's lesion being invalidating for the patient, the amputation was imperative. The tumour was measuring 6 cm large axis with skin ulceration. Histological examination shows a sarcoma proliferation of lobular and alveolar architecture. Besides, HMB45 was negative and Melan A was intensely positive.
Conclusion: Clear cell sarcoma of a manual labor's hand may become more aggressive when it is first treated as a phlegmon. Clinicians must be careful not to treat the patient only after obtaining histological proof of the diagnosis.

PS-23-031
Adamantinoma of the tibia: A case report
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Objective: Adamantinoma is one of the rarest low-grade malignant bone tumours which is predominantly located in the mid-portion of the tibia. It comprises of only 0.1–0.5 % of all primary bone tumours. The symptoms are indolent, nonspecific with slow progression of the painless swelling. Histologically, classic Adamantinoma is a biphasic tumour with epithelial and osteofibrous component intermingled with each other.
Method: Poster Presentation for case report
Results: A 22 year old male presented to Orthopaedic department with history of painless swelling in the right leg following trauma in the same leg 2 years ago. MRI showed two lesions in the right tibia. Histology showed epithelial cells arranged in islands with glandular pattern in a fibrous stroma. Immunohistochemistry showed positivity for cytokeratin and vimentin.
Conclusion: Though a rare and indolent tumour, Adamantinoma, can metastasize to lungs or recur locally, hence, a complete and sufficient surgery is necessary.

PS-23-033
Extraskeletal osteosarcoma located in abdominal wall: A case report
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Objective: Extraskeletal osteosarcoma (ESOS) is high-grade malignant mesenchymal neoplasm. It accounts for 2 % of all soft tissue sarcomas. The most common location includes deep soft tissue of the thigh (47 %), the upper extremity (20 %) and the peritoneum (17 %). In a review of the literature there are few reports of extraskeletal osteosarcoma occurring in the abdominal wall

Method: A 77-year-old woman presented with a 2 month history of right upper abdominal discomfort, nausea. A mass that is located in the abdominal wall was detected and it was removed.

Results: Microscopically, the tumour was comprised of malignant cells with osteoid production, High grade sarcoma with spindle cells showing marked pleomorphism. These findings strongly supported the diagnosis of high-grade ESOS.

Conclusion: ESOS consists of neoplastic osseous tissue that is disconnected from the skeleton and it is an unusual high-grade malignant soft tissue neoplasm with a poor prognosis. The diagnosis of ESOS should be made by using the combination of the clinical, radiographical findings and pathological verification. A careful follow up of patients with soft-tissue osteosarcoma is required because of the high rates of local recurrence and distant metastasis despite the radical treatment.

PS-23-034

Retroperitoneal solitary fibrous tumour: An unusual presentation

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Objective: Initially described as "localized fibrous mesothelioma" by Klemperer et al, solitary fibrous tumour (SFT) is a rare spindle cell mesenchymal tumour of poorly understood origin. 30 % of SFTs arise in extrapleural tissues including retroperitoneum. They rarely, if ever, metastasize but can recur locally.

Method: A case of a 29-year-old female with a retroperitoneal mass found on tomographic imaging investigating non-specific abdominal pain is reported herein. The patient had clear past medical history and normal tumour markers, while imaging with computed tomography and magnetic resonance indicated a solid retroperitoneal tumour. Surgical resection was performed.

Results: Histopathological examination revealed a well circumscribed mass with 'hemangiopericytomatous' appearance, composed of spindle-shaped cells with a 'patternless pattern'. Mitotic activity was low (<1 mitosis/10 HPF) and there was no significant nuclear atypia, while Ki-67 was 7 %. Immunohistochemistry [CD34 (+), CD99 (+), bcl-2 (+), desmin (-), S-100 (-)] confirmed the diagnosis of SFT.

Conclusion: Histologic characteristics of SFTs comprise the so-called "patternless pattern" characterized by a haphazard, storiform arrangement of spindle cells and a "hemangiopericytoma-like appearance" with prominent vascularity. According to the WHO 2013 classification, SFT and hemangiopericytoma (HPC) are now considered as one neoplasm, except for the central nervous system where meningeal HPC is still considered a separate entity

PS-23-036

Nodular fasciitis: A case report of benign lesion mimicking sarcoma

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Objective: Nodular fasciitis (NF) is a relatively common,self-limited and of unclear pathogenesis (reactive process due to trauma or even chromosomal abnormalities) benign fibroblastic-myofibroblastic lesion.It is predominantly seen in young adults(20–40 years-old) mostly affecting the upper extremities or trunk.Due to its rapid growth,rich cellularity and mitotic activity,NF is often misdiagnosed as a sarcoma

Method: A 15 years-old girl (tae-kwon-do athlete) presented to our hospital with a rapidly growing(less of 1 month),indolent mass in the left lower quadrant of the abdominal wall.Radiologic images showed a 2,8 cm well circumscribed,heterogeneously intense subcutaneous lesion.Clinically the possibility of malignancy was not excluded completely.An excisional biopsy was performed

Results: Grossly the lesion had slightly gelatinous-firm consistency.Microscopically composed of fibroblastic-myofibroblastic cells,organized in a fascicular pattern with loose and a "tissue culture" like arrangement. Absence of nuclear pleomorphism and variable mitotic activity(6/10HpF).Some areas exhibited myxoid-cystic degeneration,other were more fibrotic.Focal microhemorrhages and scattered chronic inflammatory cells were present. Immunohistochemical staining was positive for Vimentin,SMA and negative for Caldesmon,CD34,Factor XIIIa,B-Catenin, ALK,S100p,EMA,Pankeratin.According to these findings a definitive diagnosis of NF was rendered

Conclusion: Recognition and familiarity with NF can prevent a possible misdiagnosis of malignancy resulting in unnecessary treatment.Sports activities and repeat trauma (as in our case) seems to play an important causative role

PS-23-037

Undifferentiated pleomorphic sarcoma with prominent inflammation: A rare case report

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Objective: Undifferentiated pleomorphic sarcoma with prominent inflammation is the rarest type of pleomorphic sarcoma with few published series and case reports in the literature.The tumour found almost exclusively in the retroperitoneum but intra-abdominal and deep soft tissue locations have also been observed

Method: A 68 year old woman presented with a 6 month history of pain in the right hypohondrium,fever,weakness and constipation.Laboratory studies showed increased white blood cells (25.000 mm^3).Imaging studies demonstrated two retroperitoneum tumours ,one in contact with transverse colon measuring 8 cm in greatest diameter.The second tumour was lobous measuring 5 cm in greatest diameter.The tumours were resected

Results: Microscopically study from the first tumour showed morphologic and immunohistochemical characteristics [CD68(+),Vimentin (+),β catenin(+),CD20(-), CD3(-),S100p(-),actin(-),desmin(-),CD117(-),Pankeratin(-),CD34(-),ALK_1(-),CD30(-), Caldesmon(-)] that confirmed a diagnosis of undifferentiated pleomorphic sarcoma with prominent inflammation.The neoplasm associated with numerous xanthomatous cells and was invasing bowel wall. Microscopically study from the lobous tumour showed morphologic and immunohistochemical characteristics [CD68(+), Vimentin(+), Desmin(+), Actin(+), CD117(-),CD30(-),CD3(-),CD20(-),S100p(-),CD34(-),ALK_1(-),C-D15(-)] that confirmed a diagnosis of undifferentiated pleomorphic sarcoma with myogenic differentiation. After surgery the number of white blood cells was normal

Conclusion: The malignant tumour most often confused with other neoplastic or non neoplastic xanthomatous processes.Among these lymphomas,retroperitoneum-based carcinomas and dedifferentiated liposarcoma are the most common simulant

PS-23-038

Plexiform fibrohistiocytic tumour: A case report

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Objective: Plexiform fibrohistiocytic tumour (PFHT), defined by Enzinger and Zhang in 1988, is a rare soft tissue tumour of intermediate malignancy potential, that reported to be seen in children and adolescents.

Although these lesions were considered as of fibrohistiocytic origin, their histogenesis is yet to be clarified. A case has been presented diagnosed with this rare and underrecognized entity.

Method: A nodular lesion of 3,5 cm in diameter, covered with normal appearing skin was observed in an amputation material from a 54 year old female patient, resected because of a mass localized at left first toe's plantar side.

Results: Histopathological examination revealed a nodular lesion localized at subcutaneous tissue, infiltrating bone and involving distal interphalangeal joint was seen. Lesion was consisting of plump spindle cells arranged in short strands or storiform pattern, accompanied by inflammatory response.

Conclusion: Evaluated as a variant of malignant fibrous histiocytoma initially, PFHT is reclassified as a fibrohistiocytic tumour of intermediate malignant potential by World Health Organization. The entity has high local recurrence rates, though metastases are rare. No recurrence has been observed in our case after the operation.

PS-23-039

Periostin expression in chondroid tumour

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Objective: Periostin is a secreted extracellular matrix protein that is consisted by 4 fasciclin-1 domains. Periostin is secreted by osteoblast and exists on periosteum. It is involved in bone formation as a key regulator of bone microarchitecture, strength and mass. Periostin is secreted from fibroblasts in some carcinoma and metastatic lung. It is also reported that periostin is expressed in osteosarcoma and its expression level is correlated with tumour angiogenesis and poor prognosis in osteosarcoma. However, periostin expression on chondroid tumour has not reported yet. The differential diagnosis of low grade chondrosarcoma from enchondroma is important, however it is not easy. Periostin expression in chondroid tumour was analyzed in this study.

Method: Immunohistochemical stain for periostin was performed on 61 cases of chondroid tumour, including 28 enchondromas and 33 low grade chondrosarcomas. 13 cases of normal cartilage were also included as a control group. Percentage and area of positive staining were evaluated. The area was subdivided as nucleus, cytoplasm, and extracellular matrix.

Results: In contrast to all normal cartilage tissue was negative for periostin, 60 cases (98.4 %) of chondroid tumour showed positivity for periostin in any area. Considering a strong and diffuse stain pattern in most of the tumour cells achieved the best results in diagnosis of chondroid tumour (sensitivity 97.0 %, specificity 96.4 %)

Conclusion: In this study, we show the expression of periostin in chondrosarcoma and enchondroma. We suggest periostin is a novel biomarker of chondrosarcoma to distinguish with enchondroma.

PS-23-040

Diagnostic pitfalls in telangiectatic osteosarcoma

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Objective: Telangiectatic osteosarcoma (TelOS) is a rare subtype, accounting 3–10 % of osteosarcomas. It is characterised with large, nonsclerotic-lytic, destructive tumours with blood-filled cystic cavities lined by atleast focally osteoid producing neoplastic cells. Resemblance to aneurysmal bone cyst (ABC) is diagnostically concerning.

Method: We reviewed 37 specimens of 11 TelOSs and 10 TelOS-mimicking cases evaluated between 2000 and 2016. TelOS-mimickers were defined as cases with ABC-like features or extensive hemorrhage; notable TelOS-like component in biopsy specimens which is focal/lacking in resections or cases with cystic changes in postchemotherapy resections.

Results: The median age for TelOSs were 16 ± 9.3 years-old (Range:6–43 years), were more frequent in males (82 %), mostly located in proxymal tibia (46 %), humerus (36.4 %), distal femur (18.2 %), significantly involved epiphysis (83.3 %, $p = 0.06$, chi-square), with a median diameter of 10.2 ± 5 (Range: 5–17 cm). Neoadjuvant chemotherapy responce was divergent (Huvos grade I-III), however difficult to interpret for extensive cytic nature of lesion. Three cases presented with pathological fracture (28 %), two (18 %) with satellit tumours, two with accompanying ABCs. Re-biopsy/open biopsy was done in 3 cases (28 %). For other osteosarcomas with TelOS-like areas (23.8 %), metaphyseal involvement were more frequent (%60) and median age was higher (21 ± 11.6).

Conclusion: Paucity of neoplastic tissue in biopsies due to cystic nature of tumours or so-called "Hemorrhagic-necrotic variant" of TelOS with sparse osteoid production are the major pitfalls in trucut biopsies. More-confusing, conventional osteosarcomas may present with ABC/ABC-like/TelOS-like component which needs further evaluation with their affect on diagnostic outcome.

PS-23-041

Comparative analysis between growth factors of epiphyseal plate (SOX-9,Runx-2,Ihh,PTH-rP) and BCL-2 in benign and malignant cartilaginous tumours. Correlation with clinical and morphological findings

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Objective: To evaluate the expression of the growth factors of epiphyseal plate (SOX-9, Runx-2,Ihh, PTH-rP) and BCL-2 in cartilaginous tumours, correlating with histological grade and clinical outcome.

Method: 27 enchondromas, 55 conventional chondrosarcomas (CSs: 24 low grade-CS1; 31 high grade-CS2 + 3), 4 clear cell chondrosarcomas and 3 mesenchymal chondrosarcomas were evaluated. Immunostaining was applied and a score, according to Zhu et.al,2013 (modified), was used for analysis.

Results: Poor outcome was associated with high grade CSs, chondrosarcomas developing in flat bone and with SOX-9 over-expression. Higher levels of SOX-9 and Runx2 were found on cartilaginous tumours with similar morphology to growth plate. PTH-rP and Ihh higher expression levels were seen more often in enchondromas then in CSs, including when comparing with CS1, however, there was no difference of patients' outcome. BCL-2 expression levels showed no differences either in histological grade or in patients' prognosis.

Conclusion: SOX-9 may help to predict patients' outcome with these cartilaginous tumours. PTH-rP and Ihh overexpression could be useful in distinguishing enchondroma from CS1. Expression of epiphyseal plate transcription factors SOX-9 and Runx-2, in cartilaginous tumours with morphology similar to the growth plate, may suggest a possible participation of these molecules in the pathogenesis of these neoplasms. Grant:FAPESP-2015/06639-9.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-24 Thymic and Mediastinal Pathology

PS-24-001

Diagnosis of thymoma by bronchoscopic biopsy

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Objective: Thymomas, the most common neoplasms of the anterior mediastinum, can invade the adjacent structures. But the endobronchial growth of a thymoma and its diagnosis by bronchoscopic biopsy is rare.
Method: Sixty-one years old male presented with cough. The CT scan revealed a large mass lesion in anterior mediastinum invading right upper and middle lobes of lung, and pericardium. On bronchoscopic examination there were irregularities on respiratory mucosa of bronchi of right upper and middle lobes. Microscopically, beneath the intact respiratory epithelium, a biphasic tumour composed of epitheloid cells and lymphocytes was seen. Eosinophilic abundant cytoplasm , centrally located nucleus with mild atypia and syncytial growth pattern were remarkable features of the epitheloid cells of this proliferation. The epitheloid cells were positive for pankeratin, p40, pax-8, but negative for TTF1. The small cells resembling lymphocytes were positive for tdt, CD5 and other T lymphocyte markers, but negative for keratins and neuroendocrine markers .
Results: Final diagnosis was invasive thymoma with features suggestive of type B2.
Conclusion: Thymoma should be considered when a biphasic proliferation of epitheloid cells and small lymphocytes is represented on a bronchoscopic biopsy.

PS-24-002
PD1 and PD-L1 expression in thymic lesions
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Objective: Programmed death-ligand 1 (PD-L1) and Programmed death 1 (PD-1) expression has been shown in various tumours. In present study, we aimed to search the relationship of PD-1/PDL-1 expression with pathologic and clinical features in thymic neoplasms and thymic hyperplasia cases.
Method: Fifty-two cases with thymic neoplasms ($n = 44$) and thymic hyperplasia ($n = 8$) were included in the study. Cases were reevaluated in terms of demographic, clinical and histopathologic features. Immunohistochemically, PD-1 and PDL-1 antibodies were performed.
Results: Twenty-nine cases were male, 23 were female. Mean age was 45.2 (17–79 years). Most common histopathologic type was Thymoma type AB (28.8 %), followed by thymic hyperplasia (15.4 %), type B1 thymoma (11.5 %), type B3 thymoma (11.5 %), thymic carcinoma (11.5 %) and, type A thymoma (5.8 %), subsequently. Twenty-eight cases (53.8 %) had Myastenia Gravis, diagnosed in last 1 year or before. Immunohistochemically, no expression was detected by PD1 in thymic hyperplasia (0/8), whereas expression was detected in 21 of 36 thymoma cases, four of six thymic carcinoma cases. PD-L1 was expressed in 7 of 8 thymic hyperplasia, 31 of 36 thymoma, five of six thymic carcinoma cases.
Conclusion: Expression of PD1 in thymoma and thymic carcinoma cases in thymic hyperplasia give rise to immunotherapy chance in unresectable, metastatic and/or recurrent thymic neoplasm cases.

Wednesday, 6 September 2017, 09:30–10:30, Hall 3
PS-25 Uropathology

PS-25-001
High immunoexpression of EZH2 and SMYD3 in diagnostic prostate biopsies independently predicts outcome in prostate cancer patients
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Objective: Overtreatment is a major concern in prostate cancer(PCa) patients. Finding biomarkers that discriminate indolent from aggressive disease is imperative. We aim to evaluate the prognostic value of the immunoexpression of three epigenetic modifiers (EZH2, LSD1 and SMYD3) in pre-therapeutic biopsies from a cohort of PCa patients.
Method: A consecutive series of 189 patients(1997–2001) diagnosed with PCa by biopsy in a cancer center(IPO Porto) was selected. Follow-up was last updated in November 2016. Biopsies were reviewed according to most recent 2016 WHO criteria, including prognostic grade groups(GG). Immunohistochemistry was assessed using digital image analysis to increase consistency of results and cutoffs were determined based on data distribution. Endpoints included disease-specific(DSS), disease-free(DFS) and progression-free(PFS) survival.
Results: High EZH2 and SMYD3 immunoexpression associated with significantly worse DSS both in univariable analysis(HR 1.87, 95%CI 1.10–3.27; HR 2.68, 95%CI 1.02–7.92) and in multivariable analysis when adjusted for CAPRA score(HR 1.93, 95%CI 1.12–3.32; HR 2.71, 95%CI 1.04–7.10). In GG 1–3 patients, EZH2-high cases displayed significantly worse DSS when adjusted for patients' age and clinical stage (HR 3.66, 95%CI 1.15–11.60).
Conclusion: High EZH2 and SMYD3 immunoexpression independently predicts outcome at diagnosis in PCa patients when adjusted for standard clinicopathological parameters. This might assist clinicians in tailoring treatment options.

PS-25-002
PRMT1, useful immunohistochemical marker for distinguishing renal oncocytoma and chromophobe renal cell carcinoma
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Objective: Distinguishing renal oncocytoma (RO) from chromophobe renal cell carcinoma (chRCC) sometimes can be challenging. Protein arginine methiltransferase 1 (PRMT1) expression has been observed in malignancies. We investigated the potential utility of PRMT1 immunohistochemical positivity in differential diagnosis of RO and chRCC.
Method: Tumour tissue was formalin fixed, paraffin embaded and stained with hematoxylin and eosin. Immunohistochemical expression of PRMT1 was analyzed in 22 chRCCs and 15 RO. Nuclear immunohistochemical PRMT1 positivity was considered as positive.
Results: ROs showed PRMT1 immunohistochemical positivity in 11/15(74 %) cases. ChRCCs expressed PRMT1in 9/22 (40 %) cases. The significant statistical difference was proved ($p = 0{,}012$).
Conclusion: PRMT1 positivity was found in majority of ROs and minority of chRCCs. PRMT1 might be an additional immunohistochemical marker for differential diagnosis between ROs and chRCCs.

PS-25-003
The significance of intertubular growth and hilar soft tissue invasion in pure seminomas
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Objective: To study the frequency of intertubular growth and hilar soft tissue invasion (HSTI) in pure seminomas and analyze their association with other clinicopathological predictors.
Method: 49 patients with pure seminoma diagnosed between 2002 and 2017 were assessed retrospectively. We evaluated age, tumour size, lymphovascular invasion, tumour necrosis, intertubular growth, intratubular germ cell neoplasia (ITGCN) and invasion into following structures: tunica albuginea, epididymis, rete testis, hilar soft tissue.

Results: Of 49 cases, 19 (38.8 %) had intertubular growth, 26 (53.1 %) had rete invasion and 6 (12.2 %) had HSTI. On statistical analysis, intertubular growth was related to only ITGCN ($p = 0.019$) among the clinicopathological parameters. Rete invasion was correlated to lymphovascular invasion ($p = 0.14$). HSTI was significantly associated with tunica albuginea invasion and lymphovascular invasion ($p = 0.003$, $p = 0.007$, respectively).
Conclusion: Our data support that, intertubular growth pattern is not an uncommon finding in pure seminomas. The presence of intertubular growth wasn't found to be associated with clinicopathological parameters other than ITGCN. But further studies with large series are required to evaluate the significance of intertubular growth. The close correlation between HSTI and some predictive parameters, such as tunica albuginea invasion and lymphovascular invasion, demonstrate that the HSTI may be a possible predictor in pure seminomas.

PS-25-004
Recurrence variability in transitional cell carcinoma of the bladder
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Objective: Transitional cell carcinoma is a malignant tumour arising from the urothelial epithelium and may involve the lower and upper urinary tract, with proclivity for multifocality and frequent recurrence.
Method: We conducted a retrospective analysis in 71 patients with recurrent urothelial carcinoma of the bladder who underwent transurethral bladder biopsy during a period of 4 years (2012–2016).
Results: The mean age at first diagnosis was 67.4 years, with low-grade tumours in 32 cases (45.07 %) and high-grade in 39 cases (54.93 %). Regarding the initial tumour staging, 12 cases were found to be Ta (non-invasive), 43 cases T1 and 16 cases T2. Tumour recurrence was noted within 12 months of follow-up in 44 patients (61.97 %), between 12 and 24 months in 19 (26.76 %) and between 24 and 60 in 8 (11.27 %), with a mean value of 12 months, particularly 13.6 months for high-grade tumours and 10.8 months for low-grade carcinomas. Tumour grading progression was observed in 13 of 31 (40 %) of low-grade carcinoma exhibiting high-grade secondary tumour. We also found that 15 patients (12 %) had more than one recurrence.
Conclusion: These data support the progressive nature, either in grading or staging, of bladder cancer, urging a more frequent clinical follow-up.

PS-25-005
Case series of micropapillary variant of urothelial carcinoma: Tiny yet mighty
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Objective: To report a series of micropapillary urothelial carcinoma (MPUC) diagnosed at our tertiary cancer care centre.
Method: Histopathological slides of the 22 patients diagnosed with MPUC between the years 2007–2016 were reviewed. The clinical details and follow up was recorded from the electronic medical records.
Results: All 22 patients were male with median age of 62 years (range 38 to 86 years).Transurethral resection of bladder tissue (TURBT) was performed in all but one case that underwent upfront cystoprostatectomy. Cystoprostatectomy following TURBT was done in 4 cases. Characteristic morphology with retraction spaces around invasive nests of multiple papillae was seen in all cases. The stage at presentation was pT2 (11cases), pT1 (10cases) and pTa (Single case). Lymphovascular emboli were seen in six cases and nodal metastasis was observed in seven cases. Most patients were treated with non-surgical treatment in the form of neoadjuvant chemotherapy (9cases), adjuvant chemotherapy (Single case), radiotherapy (2cases) and chemoradiotherapy (3cases). Follow up was available in 16/22 cases with median follow up of 11 months (Ranging 2–113 months). Nine patients (56 %) died of the disease within 2–24 months of diagnosis.
Conclusion: MPUC is a unique variant of UC with definite male predominance and very dismal prognosis. Most patients require multimodal treatment strategies.

PS-25-006
The expression of cyclin D1 in patients with renal cell carcinoma
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Objective: The key role of cyclin D1 is regulation of cell cycle through the Rb tumour-suppressor protein. 75 % cases of renal cell carcinoma have higher expression of cyclin D1 from normal renal tissue.
Method: This retrospective study included 74 patients with renal cell carcinoma, who underwent surgery in Clinic of Urology in Belgrade. All cases were patohistologically verified in Insitute of Pathology. Immunohistochemical staining procedure for cyclin D1 was done. Real-time PCR method was used for detection of CCND gene expression.
Results: Median value for cyclin D1 immunohistochemical expression was 40 % in clear cell histological type. CCND gene duplication was found in 83,3 % of patients with clear cell renal cell carcinoma. These were statistically significant results.
Conclusion: Gene amplification correlated to immunohistochemical expression can lead us to the key point of cancer development. It can be useful to analyze transcriptional regulation of cyclin D1 expression to find out is that important in prevention and treatment of renal cell carcinoma.

PS-25-007
Multifocal synchronous bilateral Leydig cell-like testicular tumours in a young patient with clinical suspicion of adrenogenital syndrome and of Ollier disease: Just a coincidence? A case study with review of the literature
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Objective: The main differential diagnosis of testicular Leydig cell tumours(LCT) is with testicular tumours of the adrenogenital syndrome(TTAGS). Sex cord-stromal tumours(SCST) are associated with Ollier disease(OD), a rare condition caused by mutations in IDH1/2. We present a case of multifocal synchronous bilateral Leydig cell-like testicular tumours that suggested a diagnosis of TTAGS in a patient with clinical suspicion of Ollier disease.
Method: A 33-year-old male with history of bone fragility/deformities and pathological fractures presented with bilateral testicular nodules. Physical examination revealed hypospadias and tumour markers were negative. Ultrasound-guided testicular biopsy of the largest nodule(1.3 cm) was attained.
Results: Histological examination of this hilar brownish nodule showed a proliferation of cells with granular, eosinophilic cytoplasm containing abundant lipofuscin, and a fibrous stroma with adipocyte foci and lymphocytic infiltrate. The lesion was positive for alpha-inhibin, calretinin, CD99, synaptophysin and CD56, and negative for androgen-receptors. In accordance with clinical/analytical data, a diagnosis of TTAGS was suggested. Bone/cartilage disease in early age and the association with SCST raised the concern for Ollier disease, and IDH1/2 mutation screening is ongoing.

Conclusion: Pathologists must be aware of the clinicopathological characteristics that should raise the concern for TTAGS, as bilateral Leydig cell-like testicular tumours might be the first manifestation of this syndrome.

PS-25-008

Cystic nephroma - a difficult decision: A case report

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Objective: Cystic nephroma of the adult is a rare benign tumour with less than 200 cases reported worldwide. It shares characteristics with mixed epithelial and stromal tumours, considered by some authors as entities of the same spectrum of disease.
Method: We present a case of a cadaveric kidney donor with a cystic nephroma of the left kidney and make a review of literature.
Results: A cadaveric kidney donor was submitted to a pre-transplant biopsy, which showed chronic pyelonephritis, and both kidneys were declined for donation. The gross examination of the left kidney showed a cystic lesion with 1 cm of larger dimension with calcifications. The microscopy revealed a multiloculated, cystic lesion with cuboidal epithelial lining and thin septae, hyaline stroma with ovarian-like characteristics and metaplastic bone formation.
Conclusion: The present case illustrates a rare neoplastic entity being diagnosed on a transplant organ. New perspectives are arising concerning the best treatment options for patients with this diagnosis, mainly approaches based on surveillance or conservative surgery allowing to save these organs for donation.

PS-25-009

Large cell neuro-endocrine carcinoma of prostate: Report of a case and diagnostic markers

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Objective: To report a case of prostatic large cell neuroendocrine carcinoma (LNEC).
Method: A 82 year-old man presented with fatigue, weight-loss, increased azotemia and serum creatinine. Abdominal ultrasound examination showed bilateral hydronephrosis and a mass involving prostate and urinary bladder. Gleason score 5 + 5 prostatic acinar adenocarcinoma was diagnosed in prostatic biopsies in another hospital. Bladder mass was removed through transurethral resection
Results: At histological examination of bladder fragments we found a tumour composed of ribbons of large cells with prominent nucleoli, necrosis and brisk mitotic activity, that diffusely infiltrated the bladder wall. Neoplastic cells were diffusely positive for chromogranin, synaptophysin and HOXB13, and negative for prostate specific antigen (PSA), androgen receptor (AR), ETS-related gene (ERG), p63 and thyroid transcription factor (TTF-1). Ki-67 labelling index was 70 %. LNEC of prostatic origin was diagnosed. Revision of prostatic biopsy confirmed primitive LNEC. The patient died 1 month later.
Conclusion: Our case confirms prostatic LNEC has adverse outcome. Focal/absent expression of PSA, AR or ERG complicates its distinction from metastasis or local extension of NEC of other sites. This study is the first to show that HOXB13 is positive in prostatic LNEC and that it might be used as a diagnostic marker of prostatic origin in neuroendocrine tumours

PS-25-010

Large nested variant of urothelial carcinoma: A recently described, uncommon histologic variant

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Objective: Large nested variant of urothelial carcinoma (UC) was firstly described by Cox and Epstein in 2011. The aim of this report is to present histopathologic features of large nested variant of UC and to discuss the differential diagnosis by reviewing the recent literature.
Method: A 64 years old male patient was admitted to the hospital with macroscopic haematuria. Cystoscopy revealed widespread papillary tumoural lesion in the bladder. Transurethral resection was performed.
Results: Microscopic examination demonstrated surface component of low grade papillary UC and invasive, cytologically bland, large cell nests apart from each other by bulky muscular tissue. After the pathology report, radical cycto-prostatectomy and lymph node dissections were performed. Tumour histology was similar to the first material. Invasion into the prostatic stroma and peri-vesical fat were seen but the surgical margins were clear. Two metastatic lymph nodes, one in the right internal iliac and the other in the left obturator, were observed.
Conclusion: Histologically large nested variant of UC may simulate a variety of benign neoplasms. Awareness of this variant is critical, since it demonstrates the ability to metastasize and cause death.

PS-25-011

Immunohistochemical evaluation of angiogenic activity in non-invasive (pTa) bladder cancer

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Objective: The aim of this study was to establish immunohistochemical markers, useful for follow-up of non-invasive (pTa) bladder cancer (NIBC) patients. Angiogenic activity was assessed by evaluation of cytoplasmic expression of vascular endothelial growth factor (VEGF) and vascular endothelial growth factor receptor 1 (VEGFR1), in conjunction with measurement of microvessel density (MVD).
Method: The immunohistochemical expression of VEGF, and VEGFR1 was evaluated in 498 bladder cancer samples, incorporated in tissue microarrays. Microvessels were identified by immunostaining of endothelial cells for CD34. Active areas of angiogenesis were selected and MVD was presented as the average number of counted microves¬sels.
Results: After a mean follow-up of 50 months, in 498 patients diagnosed with NIBC, we found VEGFR1 expression to be an independent prognostic factor for both recurrence-free survival ($p < 0.01$) and overall survival ($p < 0.01$). In the area of dense microvessel network tumour cells showed strong VEGF and VEGFR1 positivity, however there was now significant correlation between these markers. VEGF and MVD did not have significant impact to survival rate and further outcome.
Conclusion: In this study VEGFR1 emerged as the most reliable marker for selecting NIBC patients who deserve more vigilant follow-up.

PS-25-012

A 30-month retrospective study of prostatic malignancy in younger patients: Histology, prognostic views and associated diseases

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Objective: Prostatic cancer is a well known disease described and extensively studied in older men, rarely affecting young-age. Studies of this clinical subgroup are limited, but additional data could bring a better understanding of this pathology.
Method: We set to evaluate all prostatic biopsies and surgical specimens positive for malignancy over the last 30 months in patients 55 years and younger, using the Fundeni Clinical Institute-Pathology Department's

archives. 39 patients (ages 46–55) were included and histology slides and available clinico-biological data were examined.
Results: Our study revealed that the majority of neoplasms were Gleason Score (GS): 7(4 + 3)(28.20 %), 6(3 + 3)(20.15 %) and 7(3 + 4)(17.94 %), grade groups 3, 1 and 2, respectively, predominantly with a distinct/fused glandular and cribriform histologic pattern. Based on clinico-patho-biological data main prognosis Groups were assessed for 24 patients as follows: Group IV(41.66 %), Group III(29.16 %), Group IIb(20.83 %). Anamnestic data revealed that ≈ 50 % had associated conditions, mainly cardiovascular, obesity, viral hepatitis and renal diseases. Interestingly, 8 patients were 50 years and younger and displayed GS 7(3 + 4), 5(3 + 2) and 9(4 + 5) with an overall good prognosis.
Conclusion: Our results showed different profiles: patients 50 years and younger with better patho-clinical findings and over 50 with aggressive/metastatic disease with dim prognosis. Young patients' pathologic findings should be carefully integrated in a complete clinico-anamnestic and bio-imagistic context.

PS-25-013
Histopathological presentation of sarcomatoid carcinoma of the urinary bladder: A single pathology department based cohort study
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Objective: To review the pathological features of sarcomatoid carcinoma (ScC) of the urinary bladder and to provide a retrospective image of this rare neoplastic entity in our pathology department.
Method: We performed a retrospective study of patients with a urinary bladder malignancy diagnosed in our pathology department. Our review covers the clinicopathological data between 2006 to 2017. The exclusion criteria for the study was a diagnosis of a non-urinary bladder malignancy or a diagnosis of urothelial carcinoma with no sarcomatoid component.
Results: Out of 2882 patients diagnosed with a urinary bladder tumour a total number of 30 cases met our selection criteria (1.04 %), 11 (0.38 %) patients were diagnosed with a sarcomatoid histopathological variant and 19 (0.65 %) had only a sarcomatoid tumour component (sTC). The cohort consisted of 23 males and 7 females, with a mean age of 60.1 years. Initial staging of the lesions showed: 3 pTx (10 %), 9 pT1 (33.3 %), 9 pT2 (30 %), 5 pT3 (16.6 %), and 5 pT4 (16 %). On initial presentation: 7 surgical specimens of en bloc radical cystoprostatectomies and 1 cystectomy specimen with hysterectomy with the remaining being represented by transurethral resection of the urinary bladder. On follow-up, 8 patients had local recurrences, furthermore, 4 had higher stage disease.
Conclusion: ScC of the urinary bladder is a pleomorphic cancer with a high index of variability regarding the immunohistochemical profile and remains a relatively rare primary urinary bladder neoplasm. Our results showed a small divergence from the evidence found in the literature regarding the sex of the patient and overall age of initial diagnosis.

PS-25-014
Thyroid transcription factor-1 is expressed in both invasive and non-invasive urothelial carcinomas
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Objective: Thyroid transcription factor-1 (TTF-1) has been considered as a specific marker for thyroid and lung tumours. Recent data has shown though that a wide range of neoplasms, including urothelial carcinomas, may express TTF-1. Aim of this study is investigate the frequency of TTF-1 positive urothelial carcinomas.
Method: An immunohistochemical study in a series of 40 urothelial carcinomas was performed on tissue microarrays sections (TMAs). Two more cases of urothelial carcinomas were tested in conventional slides. The first concerned a case of a non-invasive low grade urothelial carcinoma and the second was a metastatic to lung urothelial carcinoma.
Results: Out of 42 cases of urothelial carcinomas, five (11.9 %) were positive for TTF-1. Three of them concerned non-invasive papillary urothelial carcinomas and two corresponded to infiltrating urothelial carcinomas, including the metastatic one. There was no association between TTF-1 expression and tumour grade (x2, $p = 0.419$) or stage (x2, $p = 0.550$), a finding that may be biased due to the small specimen sample.
Conclusion: The observed frequency of TTF-1 positive urothelial carcinomas is higher compared to the results of previous studies. Non-invasive papillary urothelial carcinomas may express TTF-1. Pathologists should be aware of TTF-1 expression by urothelial carcinomas in order to avoid misdiagnosis, notably in metastatic disease.

PS-25-015
Clear cell papillary renal cell carcinoma: A clinicopathologic evaluation of nine cases
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Objective: Clear cell papillary renal cell carcinoma (CCP-RCC) is a newly described variant of renal cell carcinoma (RCC), consisting of clear cells arranged in tubulopapillary architecture. CCP-RCC is estimated 1 %-4 % of all resected renal tumours.
Method: We retrospectively evaluated pathological features of nine nephrectomy materials with CCP-RCC diagnosed in our center between 2013 and 2016 years. All cases were stained with antibodies against GATA3, CK7, CAIX, TFE3, RCC and AMACR.
Results: All tumours contained a single layer of clear, cuboidal cells arranged in a tubulopapillary pattern, nuclear alignments of which were away from the basement membrane. Two tumours had smooth muscle stroma. Tumour cells had diffuse CK7 and "cup-shaped" CAIX positivity. Three tumour showed nuclear reactivity for GATA3. Five tumour stained with CD10 focally. None of the tumours were stained with TFE3, RCC and AMACR.
Conclusion: CCP-RCC was included in the 2016 WHO classification. Local recurrence or metastases have not been documented among the cases reported so far. It is therefore very important to distinguish them from clear cell RCC and papillary RCC with similar morphological features. GATA3 is expressed in 30 % of CCP-RCC in our series. Unlike other variants of RCC, GATA3 positivity may contribute to CCP-RCC. Larger series are needed for showing the prognostic importance of CCP-RCC. We presented our cases for showing the importance of differential diagnosis of CCP-RCC.

PS-25-016
Hsp 90 overexpression in chronic bacterial prostatitis with corpora amylacea
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Objective: To study the expression of heat shock protein Hsp 90 in patients with chronic bacterial prostatitis (CBP) and corpora amylacea formation.
Method: Hsp90 expression was investigated in tissue of prostate of 22 CBPs with corpora amylacea by immunohistochemistry. Samples were fixed, embedded in paraffin and analized for Hsp90 accumulation using the anti-Hsp90 antibody, followed by DAB detection substrate and counterstained with Mayer's hematoxylin. Microbiological examinations were

carried out in intraoperative collection of material. The identification of accumulated bacterial cultures was carried out using conventional methods based, on morphological, tinctirial, cultural, biochemical and antigenic properties.
Results: In prostates with CBP E.coli was defined in 63.6 % of cases, S.aureus and P.vulgaris in 9.1 % of patients, Klebsiella spp. in 18.2 % of samples. CBP was characterized by significant inflammatory infiltration around glands and in the stroma. Immunohistochemical examination revealed significant expression of Hsp 90 in the prostate gland epithelium. The reaction in the stroma was observed around foci of inflammation. Corpora amylacea had a rounded shape and lamellar structure, between layers of deposits of Hsp 90 was revealed. Hsp90 overexpression was found in points corpora amylacea and glandular epithelium contact.
Conclusion: Overexpression of Hsp 90 in prostate tissue with CBP and corpora amylacea indicates a participation of the heat shock proteins in the development and formation of corpora amylacea. Hsp 90 overexpression may be regarded as a prospective (potential) role in the corpora amylacea development.

PS-25-017
Sarcomatoid mucinous tubular and spindle cell carcinoma: A rare occasion
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Objective: Mucinous tubular and spindle cell carcinomas (MTSCCs) are rare renal tumours. They account for less than 0.8 % of all renal neoplasms and have strong female predominance. Here we report an unusual case of MTSCC of the kidney with sarcomatoid differentiation.
Method: Microscopy and immunhistochemical stains were applied
Results: A 51-year-old female underwent radical nephrectomy with a radiological diagnosis of renal cell carcinoma(RCC). Macroscopically, a solid mass measuring 4.4x3.4x3.8 cm was observed without an extrarenal extension. Light microscopy revealed an epithelial tumour which consists of cords and tubules of cuboidal cells within a stroma of basophilic mucin with a spindle cell component. In addition to classical low grade areas, tumour has sarcomatoid areas characterized by the presence of large pleomorphic cells with high-grade nuclei and geographic necrosis. Immunohistochemistry for AMACR, PAX8, vimentin revealed positivity. Carbonic anhydrase IX was negative. Six months following surgery, patient is well without any problem.
Conclusion: MTSCC has been recognized as a distinct neoplastic entity. Since it usually shows an indolent behavior, it must be differentiated from more aggressive types of RCCs. Sarcomatoid differentiation is rare for this type of RCC and the prognosis is usually poor. Pathologists should be aware of the histologic spectrum of MTSCCs to ensure accurate diagnosis.

PS-25-018
Incidentally diagnosed cancer in patients undergoing benign prostatic hyperplasia related surgery - a tertiary unit experience
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Objective: Benign prostatic hyperplasia (BPH) is one of the most common male disorder in elderly population.The aim of this study is to share our experience related to the frequency of incidentally found carcinoma in patients who underwent benign prostatic hyperplasia-related surgery at the University Clinic of Urology in Skopje, R. Macedonia.
Method: Records from 1146 patients who underwent BPH-related surgery were retrieved between January 2009 and November 2016. In patients with endoscopic suspicion for bladder cancer, additional transurethral resection of bladder tumour procedure was performed. The parameters analyzed encompassed patient's age, weight of resected tissue, Gleason score (GS), pathological stage and treatment modalities. Pathological GS groups were classified into those with a GS of ≤ 6, 7 and ≥ 8. Bladder cancer groups were classified either muscle non-invasive or muscle- invasive. Eventual cause of death was classified as cancer-specific or cancer-nonspecific.
Results: Results The present study identified 1146 patients. A total of 49 patients (4,28 %) were diagnosed with cancer (3,05 % prostate cancer, i.e. 1,22 % bladder cancer). Of these, 37 patients underwent transurethral resection of the prostate, open prostatectomy was done in 10 patients, whereas simultaneous open prostate enucleation and transurethral resection of bladder tumour was performed in 2 patients. The mean weight of TUR chips resected was 6,27 g . The mean prostate enucleation weight was 59,67 g .
Conclusion: Our series demonstrate that 4,28 % of patients were found to have cancer, of these 1,83 % required additional hormonal or operative treatment. We emphasize the need of consistent communication between pathologists and urologists, for sharing the clinico-pathologic background.

PS-25-019
Oncocytic ductal prostate carcinoma with bizarre nuclei: A rare case
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Objective: Ductal adenocarcinoma accounts for 3.2 % of all prostate cancers. This cancer may exhibit several histological variations which are important to recognize to avoid misdiagnosis.
Method: A 69 year-old male patient presented with lower urinary tract symptoms. His prostate spesific antigen blood level was 72 ng/mL. A ten-quadrant transrectal ultrasonography-guided prostate needle biopsy was performed. It was diagnosed as Gleason score 4 + 5 prostatic acinar adenocarcinoma. Then,the patient has undergone radical prostatectomy.
Results: Microscopic examination reveals acinar adenocarcinoma with Gleason score of 4 + 4 with a diffuse component of infiltrating ductal adenocarcinoma with extensive areas of mucin. Remarkable oncocytic cells with bizarre nuclei and pleomorphic multinucleated giant cells were present in ductal adenocarcinoma component.
Conclusion: Recognizing of multi faces of prostatic ductal carcinoma is very important for prognosis and follow-up.

PS-25-020
A rare primary tumour of the urinary bladder: Case report
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Objective: Neuroendocrine tumours represent a small percentage of urinary bladder tumours, and are linked to molecular alterations and aberrant gene expressions.
Method: We present the case of a 46-year-old female with no clinical accusations and incidental ultrasonographic findings on routine examination. Ultrasonography revealed an ovoid, well-circumscribed sessile mass (≈ 1.5 cm diameter) of the bladder dome with endoluminal protrusion, confirmed by cystoscopy. Partial cystectomy was done.
Results: On the surgical specimen, the tumour was well circumscribed, displaying a whitish-tan cut surface. On microscopy, the tumour has a mass effect on the overlying bladder mucosa with reactive-regenerative changes and focal erosions, consisting of epithelioid polygonal cells, with centrally located nuclei, a nesting growth pattern with pushing borders

and rich fine vascular network, without necrosis/mitosis/vascular invasion. Immunohistochemical profile: chromogranin A-diffusely prostive; synaptophysin-zonally positive; PGP9.5-focally positive; AE1-AE3/GATA 3/HMB45/Melan A-negative.
Conclusion: Histopathological and immunohistochemical aspects correlated with imagistic data was characteristic for single primary bladder paraganglioma in a relatively-young patient, with no associated symptoms, stage pT2a. The patient was disease-free 8 months after resection. Primary bladder paraganglioma accounts for less than 0.05 % of bladder tumours. The literature shows increasing numbers of paraganglioma case reports/studies in the last 2 years, but further molecular and genetic studies are needed to assess risk factors, prognosis and individualised treatment.

PS-25-021
Incidental prostate cancer in TUR-P specimens: Cost/effectiveness in three tissue sampling methods
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Objective: To determine the cost/effectiveness of detecting incidental prostate cancer using three different tissue sampling methods for TUR-P specimens.
Method: We examined retrospectively all TUR-P specimens submitted in our department during 3 years: from 2012 to 2013 the specimens were entirely processed regardless of their weight (method A); from 2013 to 2014 the specimens were sampled randomly in five cassettes or less (method B); from 2016 to 2017, five cassettes were sampled for 12 grams of tissue and one additional cassette for each extra 5 grams of tissue (method C).
Results: Prostate cancer was identified in 1 of 30 (3.4 %) cases evaluated by method A, in 26 of 162 (16 %) samples evaluated by method B and in 34 of 227 (15 %) samples evaluated by method C. The median number of cassettes required per case was 10 for method A, 4.9 for method B and 7.8 for method C, with the median cost per case: 100€/case-method A, 49 €/case-method B and 78€/case-method C.
Conclusion: The cost/effectiveness ratio is most favorable for method B, having the lowest cost per case and the highest percentage in detecting prostate cancer.

PS-25-022
CDK8/CDK19 inhibition as therapeutic target of metastatic prostate cancer
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Objective: Previously, we found the Mediator subunits and kinases CDK8 and CDK19 to be highly expressed in advanced PCa and to be involved in migration and invasion. Aim of this study was to identify downstream targets of CDK8/CDK19 and to explore if their inhibition has the potential to reduce PCa aggressiveness.
Method: Immunohistochemical staining for CDK8, CDK19 and pSTAT1(Ser727), and fluorescence-in-situ-hybridization for CDK8/CDK19 were performed on a well characterized PCa cohort. PCa cells were treated with different CDK8/CDK19 small molecule inhibitors or siRNA followed by MTT, wound healing, and immunocytochemistry (ICC) and Western-Blot for epithelial/mesenchymal markers. Levels of pSTAT1(Ser727) in response to CDK8/CDK19 inhibition were measured by Western-blot and ICC.
Results: CDK8 and CDK19 were higher expressed in PCa compared to benigns, and increased in about 20 % of metastases. CDK8/CDK19 correlated significantly with nuclear pSTAT1(Ser727). We observed CDK8 or CDK19 gene amplification in 15 % of tumours. CDK8/CDK19 inhibition resulted in decreased migration, while proliferation was not affected. Mesenchymal markers and nuclear pSTAT1(Ser727) were reduced in response to CDK8/CDK19 inhibition. Small molecule inhibitors led to comparable effects as specific CDK8 and CDK19 knockdown
Conclusion: CDK8/CDK19 overexpression in PCa is based on gene amplification at least in a subset of tumours. CDK8/CDK19 inhibition leads to reduced migratory potential and mesenchymal phenotype. We identified the CDK8 phospho-substrate STAT1 as downstream signaling of CDK8/CDK19 in PCa. Collectively, this study give evidence that CDK8/CDK19 inhibition by recently published small molecule inhibitors might be a potential therapeutic option for PCa patients.

PS-25-023
Ectopic adrenal tissue in kidney: A case report
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Objective: Ectopic adrenal tissue in mid pole of kidney is extremely rare. Site of its appearance is closely related to the migration of primordial adrenal cells in the course of organogenesis. We present a patient diagnosed as ectopic adrenal tissue in kidney.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 75-year-old man suffering from urinary stone. The abdominal computed tomography showed that 21x20mm dimension cortical cyst in mid pole of left kidney. He has no abnormal blood pressure, Cushing Syndrome's signs, electrolite or hormonal imbalance. Left partial nephrectomy and excision of cyst wall in mid pole of left kidney was performed by urologist due to suspicuous for malignancy. Histopathological and immunhistochemical results were compatible ectopic adrenal tissue in mid pole of kidney.
Conclusion: Awareness for ectopic adrenal tissue in mid pole of kidney and differentiating from neoplastic lesions such as clear cell renal cell carcinoma and clear cell malignant melanoma are the main goal on it.

PS-25-025
Pitfalls in the diagnosis of prostate cancer in the era of immunohistochemistry: A retrospective review of 1394 cases
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Objective: There are few studies on the rate of over diagnosis of prostate cancer (PC). A previous study by our group from 1990 to 1996 showed an error rate of 7.5 % but with no immunohistochemistry (IHC) performed. We wished to examine a more contemporaneous series when IHC was readily available, being more relevant to current clinical practice.
Method: Core biopsies and TURPs from clinically localized PC diagnosed and managed conservatively in the United Kingdom, mostly between 2000 and 2003 were reviewed by two uropathologists. All incomplete cases where excluded and reasons for potential misdiagnosis were examined. IHC was performed centrally if needed.
Results: 1080 sets of biopsies and 314 TURPs were reviewed: 19 biopsies (1.75 %) and 7 TURPs (2.22 %) were reclassified as benign. 4 biopsies (0.37 %) were reclassified as suspicious but not diagnostic of PC. The total error rate was 2.15 %. IHC was centrally performed in 4 cases and originally on 7. The most common error on biopsies and TURPs was the overcall of areas of adenosis, followed by partial atrophy and PIN.

Conclusion: There is a significant reduction of overdiagnosis compared to our previous study. This may be the consequence of a more prevalent use of IHC and better recognition of PC mimics by pathologists possibly related to the introduction of specialist reporting. However, 23 % of the over-diagnoses in our current study had IHC originally performed and these were due to misinterpretation of the IHC findings. A low threshold for requesting IHC together with continuing education in interpretation of IHC findings may help reduce this error rate.

PS-25-027

Interobserver agreement in the assessment of tumour front inflammation and necrosis in urothelial carcinoma of the bladder

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Objective: We have previously demonstrated that tumour front inflammation and geographic necrosis are independent prognostic factors in high grade urothelial carcinoma of the bladder. Our objective was to assess interobserver variability when evaluating these two variables in this tumour type.
Method: From a cohort of 235 high grade urothelial carcinomas of the bladder, 30 cases were randomly selected for review by three pathologists. Each reviewer was provided with a single representative slide and written instructions with photographic examples depicting the scoring criteria. Tumour front inflammation and geographic necrosis were scored and binarized into high or low categories for inflammation, and positive or negative categories for necrosis. Statistical analysis was utilized to determine the degree of interobserver agreement for these variables.
Results: Interobserver variability was analyzed using Fleiss' kappa statistical analysis. Agreement was significant between the three reviewers for both tumour front inflammation (k = 0.731) and necrosis (k = 0.752).
Conclusion: Evaluation of tumour front inflammation and necrosis by 3 reviewers demonstrates significant interobserver agreement, confirming the reliability of assessing these prognostic variables in in high grade urothelial carcinoma of the bladder.

PS-25-028

Immunohistochemical assessment of the immune milieu in high grade urothelial carcinoma of bladder

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Objective: To evaluate the immunological tumour microenvironment by immunohistochemistry in a cohort of high grade urothelial carcinomas treated with cystectomy.
Method: 235 cases of high grade urothelial carcinoma of the bladder treated by cystectomy were retrospectively identified. The presence of invasive front inflammation and geographic, coagulative necrosis were documented. Tissue microarrays (TMA) were constructed from 207 cases, using 1 mm cores in triplicate. TMA sections were sequentially stained for CD3, CD4, CD8, CD20 and PD-1. PD-1 staining was scored as present/absent on infiltrating lymphocytes. CD3/4/8 and 20 were assessed by manual counting of lymphocytes in one representative high power field/core with results averaged across triplicate cores.
Results: High invasive front inflammation was noted in 76/207 (37 %) cases and geographic necrosis in 19/207 (9 %). PD-1 lymphocyte staining (any intensity) was present in 178/206 (86 %). A predominant T cell infiltrate was noted. The mean CD3 count was 67 lymphocytes/core (range 0–365) vs mean CD20 7.5 lymphocytes/core (range 0–48). The CD4:CD8 ratios were - CD4 ≥ CD8 = 104 and CD4 < CD8 = 96.
Conclusion: We demonstrate high invasive front inflammation in over one third of cases with T cells as the predominant lymphocyte. PD-1 lymphocyte expression was identified in 86 % of the cohort suggesting an immune suppressive environment.

PS-25-029

FGFR3 mutation analysis in urine samples can be used as marker of bladder cancer detection

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Objective: FGFR3 mutations are more common in superficial/papillary urothelial carcinomas and characterize a subgroup with high recurrence but good prognosis. The objective of this study is to assess whether the detection of FGFR3 in DNA from urine samples can improve sensitivity and specificity of urine cytology in the detection of bladder cancer.
Method: FGFR3 mutations were analyzed in 155 urine samples (Parc de Salut MAR, Barcelona, Spain). DNA was extracted from 3 consecutive urine samples. Mutational analysis was performed by PCR and direct sequencing. Cytological diagnosis of the respective urine samples was performed according to current standards.
Results: Eighteen of the 155 samples were mutated (11.6 %). According to the cytological classification, samples were grouped as positive (n = 14), negative (n = 32) or atypical (n = 109). Four of the 14 (28.6 %) positive, 4 of 32 (12.5 %) negative, and 10 of 109 atypical cases (9.2 %) were mutated.
Conclusion: FGFR3 mutations can be detected from urine samples. Positive cytology samples harbor a high number of FGFR3 mutations. The detection of FGFR3 mutations in negative and atypical cytology is highly suggestive of the presence of a bladder tumour, and could allow the reclassification of same negative and atypical urine samples as "positive" upon molecular classification. (FIS/Carlos III/ FEDER/ PI15/00452, Spanish Ministry of Health).

PS-25-030

Comparative analysis of prostate cancer detection on 3-Tesla multiparametric magnetic resonance imaging (3-T-mp-MRI) with histopathology on whole mount radical prostatectomies

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Objective: Due to increasing interest in focal therapy of prostate cancer (PCa) we compared histological findings in whole mount RP with 3 T-mpMRI efficacy for prostate cancer detection and localisation.
Method: Concordance for PCa localisation on PR and 3 T-mpRMI was calculated with Epidat 3.1.
Results: 58 patients with previous biopsy-proven PCa (conventional sextant approach) were analyzed. Mean age, 63 years (range 50–75 years). PCa was detected in 55 of 58 patients on 3 T-mpRMI (18 PI-RADS5, 23 PI-RADS4 and 14 PI-PADS3). Overall, 178 cancer foci were detected on RP and 79 (44,4 %) on 3 T-mpRMI while 99(55,6 %) were missed on mpMRI, 21/99 larger than 10 mm and 26/99 Gleason 7 or greater. PCa was bilateral in 51/58 cases on PR, 27/57 on core biopsy (CB) and 22/58 on 3-T-mpMRI. PCa was multifocal (more than 2 foci) on 30 PR and only 6 on 3-T-mpMRI. Kappa index for global localisation of PCa on PR vs 3 T-mpRMI was weak: 0,243 (0,192–0,295), better for PCa located on base: 0,281 (0,164–0,398) and mid prostate: 0,254 (0,174–0,333) than for PCa on the apex: 0,196 (0,118–0,275. 3-T-mpMRI detected 7/27 pT3.
Conclusion: 3-T-mpMRI missed 55 % of PCa foci, 21 % larger than 10 mm and 26 % Gleason 7 or greater. Concordance for global Pca localisation is weak, poorer for PCa in the apex.

PS-25-031

Predictive value of the new prostate cancer grading system

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Objective: Recently, a new grading System for prostate cancer was introduced by the International Society of Urological Pathology and is recommended by the WHO. Aim of this study was to analyze the prognostic value of the new Grade Groups, and whether it might reduce up-grading from biopsy to radical prostatectomy (RP)-tissue.
Method: A cohort of men undergoing radical prostatectomy from 2002 to 2015 at the Hospital of Goeppingen comprising 366 preoperative biopsies with corresponding RP-tissue, and 628 RP-specimens were re-reviewed for Grade Group and correlated with biochemical free survival (BFS), TNM,PSA, and overall (OS)/disease specific (DSS) survival.
Results: Kaplan-Meier revealed risk stratification based on Gleason and Grade Group, log-rank-test ($p < 0.001$). 5-year BFS with Gleason(Grade Group) ≤ 6(1),3 + 4(2),4 + 3(3),8(4) and 9–10(5) at biopsy were 78.6(88.3),64.0(63.4),36.2(50.3),21.6(43.7) and 0 %(21 %), respectively, and 92.8(94.9),79.1(73.7),46.0(39.7),39.4(58.8) and 20.6 %(8.8 %) at RP-tissue. Both gradings significantly correlated with TNM, PSA, OS and DSS ($p < 0.001$). Higher grade in RP-tissue compared to corresponding biopsy occured in 43 % and 33 % considering Gleason and Grade Group, respectively.
Conclusion: Our data indicate that Gleason and Grade Group predict survival, while Grade Groups do not improve predictive value and might be less sensitive in deciphering tumours with 3 + 4/4 + 3 patterns. The Grade Group system possesses less frequently an up-grading, indicating lower risk to miss aggressive tumours not represented on biopsies.

PS-25-032

HER2 expression in upper urinary tract urothelial carcinoma (UUTUC)

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Objective: Human epidermal growth factor receptor 2 (HER2) is a well-known oncogene in many malignant tumours. However, the function of HER2 is not clarified in upper urinary tract urothelial carcinoma (UUTUC). We aimed to evaluate HER2 immunohistochemistry (IHC) in UUTUC, furthermore compare prognostic significance of two criteria: the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) criteria and United States Food and Drug Administration (FDA) criteria.
Method: We produced tissue microarrays of 144 cases of UUTUC, and evaluated HER2 expression using the two criteria separately. HER2 expression were classified into low (0, 1+) and high (2+, 3+) groups.
Results: There was discrepancy of results in four cases; the following cases had 2+ using the ASCO/CAP criteria, and were reclassified as 1+ using the FDA criteria. High HER2 expression group showed significant association with International Society of Urological Pathology high grade, by both the FDA ($p = .001$) and the ASCO/CAP ($p < .001$) criteria. The high HER2 expression group using the FDA criteria was significantly associated with shorter cancer-specific survival ($p = .004$).
Conclusion: Our study indicated that high HER2 IHC has significant association with shorter cancer-specific survival, and the FDA criteria is more appropriate for interpreting the HER2 IHC in UUTUC.

PS-25-034

Predictive value of MRI guided biopsy for radical prostatectomy Gleason score, tumour volume and insignificant prostate cancer

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Objective: The efficacy of MRI-guided biopsy (MRGB) to distinguish high and low risk Prostate Cancer (PCa) is pivotal to decrease the risk of overtreatment in the low risk and insignificant (i-)PCa. The objectives are to determine overestimation and underestimation of the MRGB-Gleason score (GS) for radical prostatectomy (RP) -GS and the predictive values of MRIGB-tumour values for tumour volume (TV) and i-Pca as defined by different criteria (Epstein's criteria, Epstein's updated criteria or organ confined).
Method: Between 2006 and 2013, all patients ($N = 86$) were included who underwent both MRGB and RP at the RUMC. MRGB were scored for GS, percentage of positive cores (%PC)and tumour length (TL) and compared to RP-GS and -TV of the index tumour.
Results: The GS was underestimated in 30.2 % and overestimated in 10.5 %. The predictive value of MRIGB-GS for RP-GS and MRGB-TL for RP-TV were significant, $p = 0.000$ and $p = 0.001$ respectively, but %PC was not ($p = 0.713$). For the prediction of i-Pca, only MRGB-GS was significant for the organ-confined criteria ($p = 0.004$), but other MRGB-values were not or only marginally.
Conclusion: MRGB-GS and -TL but not %PC could predict GS and TV respectively of the RP index tumour. I-PCa could be best predicted based on the organ-confined criteria.

PS-25-035

Three-dimensional reconstruction of a bladder tumour: Histology in depth

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Objective: Histopathological analysis of transurethral resection of bladder tumour (TURBT) specimen is often challenging. Three-dimensional (3D) reconstructed histology images have the potential to aid the pathologist in visualizing the spatial arrangements and recognition of structures. The aim of this study is to explore the possibilities of staging bladder cancer by making 3D reconstructions out of TURBT specimen.
Method: Ten FFPE en-bloc TURBT specimens were sequentially cut into 30 sections of 4 μm and stained with H&E. The immunohistochemical stains Desmin and Smoothelin were used to differentiate between the muscularis mucosae and the muscularis propria. The slides were digitally scanned with a Phillips UltraFast scanner at 20x magnification. The images were aligned rigid and non-rigid using the Elastix toolbox. The urothelial cell carcinoma, the muscularis mucosae, and the muscularis propria were manually delineated by an expert observer and confirmed by a urinary tract pathologist (DSH). The 3D reconstructions were visualized with Amira software.
Results: By visualizing the combination of multiple tissue layers in a 3D reconstruction may be of value in identifying the spatial arrangement of tissue layers.
Conclusion: 3D reconstructions of TURBT specimen have the potential to help pathologists in the staging of bladder cancer.

PS-25-036

Combined alteration of ERG, prostein and PTEN identifies a subset of high grade, high stage prostate cancers with heterogeneous Gleason score in needle biopsy cores

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Objective: In a TMA with 220 patients, we found that triple hit (3-hit) ERG+, Prostein- and PTEN- is strongly associated with high grade and stage prostate cancer. In this study we investigate the relationship of needle biopsy 3-hit with grade, stage and PSA progression.
Method: Thirty one ERG+ patients with available biopsy, prostatectomy and follow-up data were selected. Immunohistochemistry for ERG, Prostein and PTEN was performed in all the positive cores.
Results: ERG was positive in 30/31 patients (97 %), Prostein- in 23/31 (74.2 %) and PTEN- in 16/31 (51.6 %). From 23 patients with more than one positive core, 20 (87 %) were ERG+ in all cores, 7 (30.4 %) Prostein- and 14 (60.8 %) PTEN- ($p < 0.0001$). The 3-hit was present in 12/15 (80 %) patients with heterogeneous Gleason score (GS) in the different cores and in 2/8 (25 %) with homogeneous GS ($p = 0.038$), with PPV = 85 % and NPV = 66.6 %. The 3-hit was present in 12/19 prostatectomy GS > 7 cases, 4/11 GS7 and 0/2 GS6 ($p = 0.09$). It was more common in pT3 (60 %) and cases with progression (35.7 %).
Conclusion: ERG, Prostein and PTEN may provide valuable information as 3-hit is associated with heterogeneous GS at biopsy, and related to high grade and stage at prostatectomy, and progression. FIS/CarlosIII/FEDER/PI15/00452, Spanish Ministry of Health.

PS-25-037

Xp11 translocation renal cell carcinoma with NONO fusion partner: Analysis of 4 cases

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Objective: Xp11 translocation renal cell carcinoma (TRCC) is characterized by translocation involving the gene TFE3 and different fusion partners. It was found that association between TFE3 and several fusion partners has a morphologic correlation. TFE3-NONO TRCCs were discussed recently.
Method: Four cases of TFE3-NONO TRCC were selected of 42 Xp11.2 TRCCs in our registry. These cases were examined using immunohistochemical stainings and FISH.
Results: Patients were 2 males, 2 females, age ranged 37–86 years (median 57.5), size range 0.8–6 cm (median 3.9). Three cases have papillary architecture, composed mostly of clear cells with microcalcification. In one case tumour resembled urothelial carcinoma by architecture and by cytology. All cases were variably reactive for AMACR and PAX8. FISH confirmed translocation TFE3-NONO in all cases.
Conclusion: TFE3-NONO TRCCs have distinct morphology, mostly papillary architecture and clear cell population with subnuclear vacuoles leading to distinctive nuclear palisading. However, subset of TFE3-NONO TRCC can resemble urothelial carcinoma. In contrary to generally accepted opinion TFE3-NONO TRCC can occur also in elderly patients.

PS-25-038

ARID1A immunoexpression is not prognostic in high grade urothelial carcinoma of bladder

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Objective: ARID1A is a tumour suppressor protein with prognostic significance in tumours with dual pathway models of carcinogenesis, such as endometrial carcinoma or epithelial ovarian carcinoma. Given the bimodal pathway of cancer development in urothelial carcinoma of the bladder, we hypothesized that a similar prognostic relationship may be seen in the high grade pathway of this tumour type.
Method: A triplicate core tissue microarray was created from 207 high grade urothelial carcinomas treated with cystectomy. Sections were stained with ARID1A (rabbit polyclonal, Sigma Aldrich, 1:100 dilution) and scored as 0 (negative), 1 (weak stain<intensity of stromal cells), 2 (moderate intensity), 3 (strong intensity) with results averaged across all cores. Relapse free and disease specific survival data were calculated (Chi square, Fisher's exact tests).
Results: 206 cases were evaluable, scored as 0 (8), 1 (22), 2 (98) and 3 (78). Results were binarized: 0 vs 1,2,3 and 0/1 vs 2/3. Neither method showed any association between ARID1A and stage, vascular invasion, nodal status, age, tumour size, relapse free or disease specific survival ($p > 0.05$).
Conclusion: No association was identified between ARID1A protein expression and cystectomy parameters or oncologic outcomes. ARID1A may be more relevant in the low grade pathway of urothelial carcinogenesis.

PS-25-039

Three-dimensional architecture of prostate cancer growth patterns

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Objective: To elucidate the 3D architecture of prostate cancer growth patterns.
Method: Fifteen individual 0.5 mm punches were taken from archival prostatectomies and fluorescently stained with CK8-18 and CK5 antibodies. After clearing with benzyl alcohol: benzyl benzoate (BABB), tissues were imaged using a confocal microscope with long working distance.
Results: Generally, prostate adenocarcinoma consisted of interconnecting tubules lined by luminal cells. Gleason pattern (GP) 3 tubules had a mean diameter of 45 μm (SD 13 μm), with which fused GP4 formed a continuum showing condensed anastomosing glands. Ill-formed GP4 tubules (average diameter 24 μm, SD 7 μm) showed enhanced branching and anastomosis. GP5 cords (average diameter 12 μm, SD 3 μm) consisted of single cells with interconnecting tubules and diminishing lumina. Cribriform GP4 and solid GP5 represented large epithelial proliferations without intermittent fibrovascular stroma either with or without round and linear lumina, respectively, not connecting with other growth patterns. Glomeruloid GP4 revealed two growth patterns: intraluminal epithelial proliferations continuous with cribriform GP4 and strongly curving glands in close relation to GP3 and fused GP4 glands.
Conclusion: Novel three-dimensional microscopic imaging gives comprehensive insight in mutual relations and key features of clinical prostate cancer growth patterns.

PS-25-040

The association between expression of P16 and Her2/neu immunostainings, grading and prognosis of urothelial cell carcinoma of the bladder

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Objective: The present study was aimed to evaluate association of positive P16 and Her2/neu immunostainings with tumour grade and prognosis.

Method: The study was performed on 412 samples obtained from patients suffered from urothelial carcinoma in tissue microarray paraffin blocks. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20 % of cells with expected count of less than 5 were observed. Quantitative variables were also compared with ANOVA test or Kruskal-Wallis H test. For statistical analysis, SPSS version 16.0 was used.
Results: Expression of Her2/neu was higher in high grade than low grade tumours (H score: 167.69 ± 103.77 versus 93.16 ± 77.06, $p = 0.001$). Using the ROC curve analysis, Her2/neu could discriminate high grade from low grade successfully (AUC = 0.710). The best cutoff value for Her2/neu to differentiate high grade from low grade tumours was 95.0 yielding a sensitivity of 74.4 % and a specificity of 55.2 %. The mean H score for P16 marker was 52.22 ± 89.71 in survived group and 98.93 ± 107.00 in non-survived group that was significantly lower in survived ones ($p = 0.031$).
Conclusion: By P16 and Her2/neu markers, poor prognosis and high-grade urothelial carcinomas can be predicted respectively.

PS-25-041
Somatic type malignancy in the retroperitoneal metastases from testicular germ cell tumours
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Objective: Our aim in this study was to evaluate the cases with somatic malignancy (SM) occuring in retroperitoneal metastases from testicular germ cell tumours (GCTs).
Method: Data on all patients with orchiectomy due to GCTs and retroperitoneal metastatectomy (RM) afterwards between 2000 and 2016 in a single institution were collected ($n = 153$). Pathological review and survival analysis were performed.
Results: 78 RM contained no viable tumour while 46 metastatectomies consisted of only teratoma. Non-teratomatous GCT was present in 22 tumours . SM was observed in 7 RMs (2 pleomorphic sarcoma, 1 rhabdomyosarcoma, 1 myofibroblastic sarcoma, 1 PNET and 2 adenocarcinoma). Their corresponding testicular primaries were pure teratoma in ($n = 1$), teratoma with sarcomatous transformation ($n = 1$), pure Yolk sac tumour ($n = 1$) and mixed GCTs ($n = 4$ (3/4 containing teratoma component and 2/4 with accompanying sarcomatous areas)). Overall, 13 patients died of disease, among which 3 were in the group which had SM in metastases.
Conclusion: Patients with no viable tumour or with only teratoma in RMs have a lower mortality rate than those with non-teratomatous components. Occurrence of SM is rare (4.5 %) but indicates the worst prognosis with 35.7 % death rate. Teratoma with or without somatic-type malignant component is the most common germ-cell element in their corresponding testis primaries.

PS-25-042
Impact of micropapillary carcinoma variant proportion on prognosis in urothelial carcinoma of the bladder
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Objective: The aims of this study were to investigate the incidence of micropapillary urothelial carcinoma(MPUC)among urothelial carcinoma(UC)patients treated by radical cystectomy and to identify the morphological parameters predicting its poor outcome.
Method: This study presents a pathological analysis of all cases of MPUC of the bladder diagnosed between 2010 and 2016 with cystectomy specimens for evaluation.Tumours were stratified on the extent of MPUC:focal,<10 %;moderate,10–50 %;extensive,>50 %; and this was correlated with morphological prognosis factors including tumour stage,and lymphovascular invasion.
Results: Thirty-five MPUC patients were identified,18 % of all UC of the bladder($n = 188$). Median age was 63.6 years (48–76 years) with the majority of the cohort presenting with high-grade(94.3 %), muscle invasive or locally advanced disease (91.4 %) and lymphovascular invasion(88 %).All cases with extensive MPUC ($n = 14$)were of a high pathological stage (pT2,pT3 or pT4)and were associated with lymphovascular invasion.Among moderate MPUC cases($n = 12$),91.6%were at least pT2 and 91.6 % showed lymphvascular invasion. Thirty-three percent with focal MPUC (3 of 9cases) were pT1 and 44.4 % had lymphovascular invasion.
Conclusion: MPUC is a highly aggressive variant of UC in which the prognosis is related to the proportion.Cases with moderate or extensive MPUC are at high risk of being advanced at presentation.

PS-25-043
TMPRSS2-ERG differentiates towards low-grade prostate cancer but is not an independent predictor for clinical outcome
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Objective: The TMPRSS2-ERG gene fusion is the most common gene rearrangement in prostate cancer and the main reason for overexpression of ERG. Although the clinical significance of TMPRSS2-ERG is yet to be proven, the presence of the fusion gene is a key genomic event specific for prostate cancer. In the present study we aimed to investigate the relation between ERG-expression and 2 parameters: Gleason grade and clinical failure (CF, i.e. disease recurrence).
Method: Matched patient cohorts were composed for different Gleason grades and for presence/absence of CF 5 years post-prostatectomy. Tissue micro-arrays with both PCa and non-PCa tissue were composed and processed for immunohistochemistry with a clinically validated ERG-antibody. Stained slides were digitalized, epithelium was selectively annotated and analysed for percentage of (nuclear) ERG-expression with standardized and validated image analysis, followed by statistical analysis.
Results: We observed a significant decrease of ERG expression in the Gleason 8 group as compared to the Gleason 6 and 7 groups. No significant differences in ERG expression were observed between the CF and the non-CF groups. There was high intra-tumoural heterogeneity in ERG expression (as measured by the coefficient of variation across the samples of each patient).
Conclusion: The present results indicate that TMPRSS2-ERG differentiates towards a low grade phenotype of prostate cancer. No evidence was found for TMPRSS2-ERG as an independent predictor for clinical outcome. The high intra-tumoural heterogeneity in ERG-expression suggests prominent tumour clonality in TMPRSS2-ERG gene fusion in PCa. The present data show that decreased ERG expression might be useful as a clinical biomarker for aggressive PCa.

PS-25-044
NPY system in prostate cancer neuroinvasion
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Objective: Peripheral nerve infiltration is often found in prostate cancer, being one of dissemination ways, but also it probably stimulates neoplastic cell survival. Mechanisms of cancer neuroinvasion are not well recognized, some studies suggest NPY as one of players. In this study Neuropeptide Y (NPY) and its receptors system in prostate cancer (CaP) was evaluated.

Method: The study was performed on 51 archival cases of CaP, benign prostate tissue served as a control. Tissue microarrays were manually constructed including finally 150 tissue cores. Immunohistochemical technics were carried out with standard procedures using commercial antibodies (NPY, Y1R, Y2R, Y5R). Analysis of NPY system elements expression comprised qualitative and quantitative assessment by two independent pathologists. Patho-clinical data included patients' age, pTNM stage, Gleason grade and grade group. In CaP cases, NPY system reactivity was compared between tumour tissue and neuroinvasion areas.
Results: All CaP cases presented NPY and its receptors expression within the neoplastic cells. Both NPY and its receptors showed higher expression with different cellular distribution in cancer then in BPH. NPY system presented statistically significant higher expression in areas of neuroinvasion then in central parts of cancer mass (Wilcoxon test $p < 0{,}001$ for all). NPY system reactivity was also higher in extraprostatic extension then in central parts of tumours.
Conclusion: NPY system is expressed in CaP tissue, being involved in neoplastic progression and neuroinvasion.

PS-25-045
Specificity and sensibility of old and new markers for germinal cell tumour
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Objective: Germinogenous testicular tumours are a disease of young men of working age. Correct and speedily diagnosis leads to effectiveness of treatment.
Method: The material of the study was 87 cases of testicular tumours, patients who received surgical treatment at the Petrov Oncology Institute for the period from 2001 to 2016. Histological HE slides were scanned and prepared TMA blocks and stained with CD30, Glypican-3, CD117, Oct3 / 4, PLAP, Podoplanin, SALL4.
Results: The average age of the patients was 32 years. Histology diagnosis were: seminoma in 49.5 %, non-seminary germ cell tumour of more than one histological type (mixed) - 28 %; embryonic cancer - 14 %; teratoma and yolk sac tumour were met in 2 % and the remaining 4.5 % were choriocarcinoma and spermatocytic tumour — SALL4 is the most sensitive marker for germ cell tumours. The sensitivity of oct3 / 4 for seminomas is 89 %, for embryonic cancer 91.5 %, PLAP for seminomas is 79 %, for embryonic cancer 77 %; Specificity for seminoma and embryonic cancer 93.5 %. The most sensitive and specific markers for seminoma are D2-40 and CD117. The sensitivity of CD30 for embryonic cancer is 94 %.
Conclusion: The use of TMA technology to identify germicogenic testicular tumours has a comparable effectiveness with conventional

PS-25-046
Squamous cell carcinoma (SCC) of the penis: A retrospective study of 55 penectomies
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Objective: To investigate the clinical and histopathological features of squamous cell carcinomas (SCC) of the penis in penectomies specimens.
Method: Patients with SCC that underwent penile penectomy were identified in the files of our Department of Pathology. These surgeries were performed during a period of 30 years (1986–2016). The histological review was done according to the last WHO classification (HPV related/non related). Depth of infiltration, perineural and vascular invasión was reviewed. Patients were re-staged according to the 8th edition of the AJCC.
Results: 55 male patients, with a mean age of 63 years (26–94). Most of our cases were diagnosed of usual penile SCC, other variants identified were basaloid, verrucous and warty variants. 22 % were Grade III, 50 % Grade II and the rest Grade I. At follow-up, 3 patients (1 %) died of causes related to the disease, they had a usual SCC (grade II or III) and lymph node metastases in 2 of the cases.
Conclusion: Squamous Cell Carcinoma of the penis, is a neoplasia with a low incidence in our country. In our serie the most common type was usual SCC (non related to HPV). Our results are similar to those described in the literature.

PS-25-047
A case report: Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma
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Objective: Hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma is a rare and relatively newly defined entity. It has characteristic histological features and specific germline FH mutations.
Method: Case report
Results: Herein, we report a case of a female patient with a history of multiple uterine leiomyoma. The patient subsequently presented with a right renal tumour. Histology of the renal tumour and genetic testing confirmed hereditary leiomyomatosis and renal cell carcinoma-associated renal cell carcinoma. During genetic counselling, a family history of renal cell carcinoma and uterine leiomyoma was revealed.
Conclusion: We hope to raise the awareness of this entity to pathologists and clinicians in order to confidently arrive at the diagnosis and facilitate appropriate further management.

PS-25-049
Primary renal embryonal rhabdomyosarcoma in young adult
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Objective: Primary renal rhabdomyosarcoma (RMS) is an uncommon tumour and only rare cases have been reported in adults. We report an unusual case of primary embryonal RMS of the kidney in a young male.
Method: A 22-year-old man presented with left flank pain. Ultrasound and CT-scan demonstrated a large mass occupying the left kidney and multiple lung nodules. Left radical kidney resection was performed.
Results: Gross examination showed a nodular tumour (13x12x9cm) with solid and myxoid-gelatinous areas. Multiple neoplastic nodules in the renal/perirenal fat and a large embolus in the renal vein were identified. Pathology revealed a mesenchymal neoplasm with hypo- and hypercellular areas in a loose, myxoid stroma, with focal botryoid pattern. Tumour composed of medium-large rounded, stellate or spindle cells with scant cytoplasm, few rhabdomyoblasts and tadpole cells and some hyperchromatic multilobulated cells with atypical mitoses. Immunohistochemistry demonstrated positive staining for desmin (70 %), MSA (30 %), myogenin (15–20 %), WT-1(cytoplasmic), SMA (25 %), vimentin and p53. The diagnosis of renal ERMS with focal anaplasia (Group 1 WHO)/TNM Stage 4 was made.
Conclusion: Primary renal ERMS in adults is an extremely rare tumour with poor prognosis, arising from skeletal muscle progenitor cells. It must be incorporated in the differential diagnosis of renal sarcomas.

PS-25-051
Pilomatrixoma-like testicular tumour without teratomatous elements: Case presentation and review of the literature
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Objective: Pilomatrixoma is a benign tumour of skin appendages with a low incidence. Only four cases reported in the literature in this location, three of them have reported teratomatous elements. We report, to our knowledge, the second case of Pilomatrixoma-like testicular tumour without teratomatous elements.
Method: A case of 38 years old man with a left testicular lump and discomfort since 5 months. No changes in size has been observed. Testicular ecography showed a calcified sub-capsular tumour of 1.5 x1.5 cm. and reported a suspected testicular tumour. Left orchiectomy was performed.
Results: Gross examination of left testicle showed a whitish stony tumour of 1.5 x1.5x1.3 cm. Tumour was decalcified. Gross sections showed a solid mass with fibrous calcified areas. Whole tumour mass was included for microscopic study that showed a mature laminar bone tissue with fibrous stroma with numerous histiocytes and mature lymphocytes. Central hialin material and ghost cells were observed. No basaloide epithelial cells nor teratomatous elements or testicular intraepitelial neoplasia were observed.
Conclusion: Pilomatrixoma-like lesion is exceptionally rare in this location. With few cases reported in the literature it is difficult to make a solid conclusions. Nevertheless, we agree with authors who consider it as a monodermal mature teratoma. We recommend a comprehensive study of a surgical specimen and tumour in search for teratomous elements.

PS-25-052
Relation of renal cell carcinoma (RCC) subtypes and prognostic grading to stat-3 expression
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Objective: The Stat-3 (Signal transducer and activator of transcription) gene is part of a family known as the STAT genes. These genes provide instructions for making proteins that are part of essential chemical signaling pathways within cells. This protein is involved in many cellular functions. It regulates genes that are involved in cell growth and division, cell movement.In additon to, it regulates self-destruction of cells (apoptosis). It is known that nuclear grade (Fuhrman) and subtypes affect survival in renal cell carcinomas. In this study, Stat-3 relationship will be tried to be revealed with renal cell carcinomas (RCC).
Method: 41 RCC cases were taken for this study. The cases were 26 clear cell RCC (CCRCC), 7 chromophobe cell RCC (ChRCC), 8 papillary RCC (PRCC). 12 of the CCRCC lesions were grade 1. 5 of the CCRCC lesions were furhman grade 2. 9 of the CCRCC lesions were furhman grade 3. Stat-3 was assessed as both prevalence and intensity of staining. Scored between 0 and 3. The staining pattern was cytoplasmic and apical staining was observed.
Results: No significant correlation was found with furman grade. The staining rate of CCRCC was 1.7, the staining rate of ChRCC was 1.3, and the staining rate of PRCC was 2.1.
Conclusion: In this study stat 3 staining was thought to be related to RCC subtypes. Clear cell RCC may be furhman grade 1 at 46 % of cases because of low staining.

PS-25-053
Pulmonary giant cell carcinoma kidney metastasis
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Objective: We present a case of pulmonary giant cell carcinoma that metastasized to the left kidney.
Method: A 77-year-old female with a history of giant cell carcinoma of the lung as well as ductal breast carcinoma. She presented with 3 month history of hematuria, CT scan revealed a 3.1 cm tumour in the upper pole of the left kidney. The patient underwent a left nephrectomy. On gross examination the resected specimen consisted of a white-yellow tumour measuring in maximum diameter 3.4 cm with infiltrative borders located in the renal medulla and renal pelvis.
Results: On microscopic examination there was extensive infiltration consisting of solid nests as well as scattered giant cells. Nuclei were large, pleomorphic and sometimes bizarre. Areas of conventional adenocarcinoma, squamous cell carcinoma or spindle cells were not identified. The differential diagnosis included renal cell carcinoma and metastasis from the known pulmonary sarcomatoid carcinoma or breast carcinoma. Immunohistochemistry was positive for TTF-1, CK-7, and negative for Vimentin, CD-10, GATA-3.
Conclusion: The diagnosis of metastatic pulmonary giant cell carcinoma was made. Pulmonary giant cell carcinomas are rare neoplasms, comprising approximately 1 % of all non–small cell lung cancers. Their clinical behavior is extremely aggressive.

PS-25-054
Incidental prostate cancer at radical cystoprostatectomy for bladder cancer
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Objective: Prostate cancer (PCa) incidentally discovered at radical cystoprostatectomy (CP) is reported with variable prevalence rates. Its clinical relevance remains questionable as prognosis at the time of diagnosis usually depends on bladder cancer stage.
Method: We performed a retrospective study of 242 radical CP for bladder cancer between march 2008 and march 2017 at our hospital. Histopathology reports were screened for both bladder and prostate characteristics according to the current classifications (WHO 2016, TNM 2010).
Results: PCa was displayed in 46 of the 242 CP (19 %).Mean age was 67 years old. Bladder cancers were mainly urothelial carcinoma ($n = 38$). Bladder cancers were mainly T3 (45.6 %) and stage IV (30.4 %). Prostate was partially embedded in 41 cases (89.1 %) and completely embedded in 5 cases (10.9 %). All PCa were adenocarcinoma. Five cases displayed prostate intraepithelial neoplasia. Whether completely embedded or not, prostate adenocarcinoma was mainly T2a ($n = 32$) and grade group 1 ($n = 35$).
Conclusion: Patients' prognosis depends on bladder cancer as they present with advanced stages. Complete embedding of the prostate doesn't seem to increase PCa detection and isn't associated with a higher grade group or stage. A larger cohort studies are required to validate our results.

PS-25-055
Antopol-Goldman lesion: Two case reports
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Objective: An Antopol-Goldman lesion or subepithelial pelvic hematoma of the kidney is a rare cause of hematuria that may clinically mimick a renal or a pelvic neoplasm. We present two cases of female patients, 83 and 89 years old, with gross hematuria.
Method: The patients presented clinically and radiologically as upper urinary tract tumours and underwent nephroureterectomies. On gross examination there was no evident tumour only large subepithelial hematomas in the pelvic area, 3 and 4,5 cm in diameter in each case.
Results: We examined microscopically the whole pelvic area of the two cases and performed excessive sampling of the rest kidney parenchyma

but there was no evidence of a tumour neither of atypia or dysplasia of the urothelium. The only microscopic finding was of subepithelial organizing hematomas in the pelvic region.
Conclusion: Subepithelial hematoma of the renal pelvis (Antopol-Goldman lesion) is a benign lesion which simulates an upper urinary tract urothelial tumour, both clinically and radiologically, and so is usually treated. Its etiopathogenesis probably is a multifactorial process. Knowing this entity is necessary to avoid unnecessary nephrectomies.

PS-25-056
PIN-like prostatic duct adenocarcinoma in a resource limited setting: Haematoxylin & eosin diagnosis
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Objective: This study aims to report rare variants of ductal adenocarcinoma
Method: A 4-year retrospective study of PIN-like prostatic duct adenocarcinoma diagnosed between January to December (2013–2016) in the Department of Pathology/Forensic Medicine, University of Abuja Teaching Hospital, Gwagwalada, Abuja. The materials consisted of tissue blocks, glass slides and duplicates histopathology reports of patients whose specimens were received and processed in the Histopathology Laboratory of the hospital. The diagnosis was made by Haematoxylin & Eosin stained glass slides, no immunohistochemistry was done due to limited resources in our center at the time of this study.
Results: Twelve (12) Pin-like adenocarcinoma of the prostate were studied. The age range of the patients was 49–75 years with the mean age of 62 years.
Conclusion: The import of this study is to show that with high index of suspicion and in-depth study of histopathology, rare variants of prostatic ductal carcinoma can be made in a resource limited setting.

PS-25-057
ISUP vs Fuhrman grading in renal cell carcinomas: Experience in a community hospital
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Objective: Review of 57 consecutive cases(16 females-64 years old-, 41 males-61 years old-) with clear cell carcinomas studied at our hospital . We regraded every case using the Fuhrman and ISUP system.
Method: Distribution of cases by grades were as follows; Fuhrman:12G1,26G2,12G3,7G4. ISUP:31G1,10G2,9G3,7G4. Distribution by stage and grade system: pT1*n* = 38: Fuhrman-9G1,22G2,7G3. ISUP.-26G1,7G2,5G3. pT2*n* = 4: Fuhrman-2G1,1G2,1G3. ISUP-2G1,G2,G2. pT3*n* = 14:Fuhrman-G1,2G2,4G3,7G4. ISUP-3G1,1G2,3G3,7G4. pT4*n* = 1:1G2Fuhrman and 1G2ISUP. Size was the same for G4 in both systems and similar for G3. G2 ISUP were bigger than Fuhrman's (5.3 cm vs 4.1 cm) while G1 ISUP tumours were smaller than Fuhrman's (3.8 cm vs 4.1 cm).
Results: High grades showed no differences between both systems (G4 are 100 % pT3 with ISUP or Furhman and G3 are very similar in stage and size with both systems). However G1 shows smaller size (3.8 cm vs 4.1) and lower stage with ISUP (83 % G1 ISUP vs 75 % G1 Furhman are pT1) while G2 following Furhman has more incidence of pT1 (70 % G2 ISUP vs 84 % Furhman).
Conclusion: In our series ISUP G1 seems to correlate better with pT1 than G1 Fuhrman, while for high grades (G3 and G4) differences are not significant.

PS-25-058
Primary retroperitoneal seminoma presenting as renal tumour
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Objective: Germ cell tumours primary in extragonadal sites are rare tumours, which can occur in the retroperitoneum. In particular, retroperitoneal seminoma account for 2 % of all germ cell tumours, less than 100 cases described in literature. Lack of knowledge of this condition, together with its rarity, can result in diagnostic delay.
Method: The aim of this study is to underline the diagnosis challenges of such a rare tumour. We reported the case of a 68-years-old male patient with an advanced retroperitoneal seminoma involving also the kidney, which was presented like a renal tumour.
Results: Patient undergo surgery with removal of the left kidney, paraaortal lymph nodes and left adrenal gland. Histopathological and immunhistochemical studies revealed a seminoma of the usual type. The patients tumour markers were investigated (LDH, betaHCG, alfaFP). In addition, testicles were examined using ultrasound scan.
Conclusion: Although retroperitoneal seminoma is rare, this entity should be taken into account in the differential diagnosis of a male patient presenting with a retroperitoneal mass. The histopathological analysis is crucial for an accurate diagnosis and a proper management strategy.

PS-25-059
Urachal adenocarcinoma: A case report of rare entity
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Objective: Urachal carcinoma accounts for 0.2 % of all bladder cancers, theoretically derived from glandular metaplasia of the urachal epithelium. Non-cystic adenocarcinomas are the most common, being the enteric type morphologically identical to colorectal adenocarcinoma.
Method: We report the case of a 55-years-old male with complaints of hematuria and suprapubic discomfort. Ultrasonography revealed a cystic lesion with 47 mm, in the median anterior abdominal wall, with thickening of the inferior part, extending to the bladder's dome, suggestive of malignancy.
Results: Gross examination revealed a tumoural mass in the anterior abdominal wall/bladder dome, with 8 cm, with cystic and solid areas. Microscopy showed an infiltrative tumour localized in bladder dome, in continuity with the cyst of the anterior wall. Cystitis cystica, cystitis glandularis and carcinoma in situ were excluded. Surgical margins were negative. Neoplastic cells had strong and diffuse positivity to CDX2 and focal staining to CK20. CK7, 34 Beta-E12 and nuclear staining to B-Catenin 14 were negative. The final diagnosis was an urachal adenocarcinoma, enteric type, with extension to the bladder, staged IIIA (Sheldon staging system).
Conclusion: Owing to its rarity there are no protocols for adjuvant treatment, and our patient was treated solely with surgery. After 5 months he is alive, without tumour relapse.

PS-25-060
Prostate cancer patients with overall and highest biopsy Gleason score 3 + 4 = 7 have similar outcome
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Objective: To investigate the relation and clinical outcome of prostate cancer patients with overall and highest Gleason score (GS) 3 + 4 = 7 at diagnostic biopsy.
Method: Prostate cancer biopsies from the European Randomized Study of Screening for Prostate Cancer (ERSPC) were revised according to WHO/ISUP 2014 (n = 1031). Overall GS 3 + 4 = 7 considered all biopsies cores as one, which might include individual biopsy cores with GS 4 + 3 = 7 or 4 + 4 = 8; highest GS 3 + 4 = 7 excluded cases with individual biopsy cores with higher GS.
Results: In total 370 patients had overall GS 3 + 4 = 7, of whom 310 had highest GS 3 + 4 = 7 in any of the cores. Men with overall GS 3 + 4 = 7 with at least one core with GS 4 + 3 = 7 or 4 + 4 = 8 (n = 60; 16 %) had higher age, Prostate Specific Antigen (PSA) level, number of positive biopsies, % tumour involvement, % Gleason grade 4 and cribriform growth (all $p < 0.05$). In multivariate Cox regression analysis, biochemical recurrence-free survival of men with highest>overall GS 3 + 4 = 7 was not statistically different from those with highest = overall GS 3 + 4 = 7 after radical prostatectomy (p = 0.33) or radiotherapy (p = 0.40).
Conclusion: Men with overall GS 3 + 4 = 7 at biopsy including separate cores with higher GS do not have worse biochemical recurrence than those with maximum GS 3 + 4 = 7.

PS-25-061
A rare case of Xp11 translocation renal cell carcinoma-TFE3
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Objective: MiT family translocation renal cell carcinomas harbour gene fusions involving either TFE-3 or TFEB transcription factor genes. TFE3-Xp11 translocation carcinoma is mainly associated with Xp11.2 chromosomal translocation. It constitutes about 1–1.6 % of adult RCCs (mean age: 35 years old). We present a rare case of TFE-3 translocation RCC arising in the cortex of the renal parenchyma of a 32 year old man.
Method: A renal mass was diagnosed incidentally, in a young male with no remarkable symptoms. A left total nephrectomy was performed. The surgical specimen was formalin –fixed and processed for histopathological study.
Results: Gross examination revealed a cortical mass sized 3x3x2.5 cm invading the renal sinus fat. Histology revealed papillary-pseudopapillary and solid, alveolar growth pattern of enlarged neoplastic cells with clear or granular eosinophilic cytoplasm, occasional small nucleoli and well defined cell borders. Psammoma bodies and hyaline globules were also present. Immunohistochemically, tumour cells stained strongly for PAX8, AMACR, CD10 and focally for TFE-3. According to WHO/2016 the diagnosis of MiT family translocation renal cell carcinoma - TFE3 was established.
Conclusion: The diagnosis of MiT family translocation renal cell carcinoma should be considered whenever we have a young patient with the above mentioned microscopic findings.

PS-25-062
Signet ring cell prostatic carcinoma displaying pagetoid spread
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Objective: We report a case of signet ring adenocarcinoma (SRA) of the prostate associated with intraductal carcinoma (IC) and pagetoid spread (PS).
Method: A 63-year old patient was admitted to our hospital due to hematuria. Serum PSA was elevated. A biopsy was performed with a diagnosis of prostatic adenocarcinoma Gleason score 10 with signet ring features. A radical prostatectomy was performed.
Results: Histologically there was an extensive infiltration of the prostate mostly by single cells without cohesion with signet ring morphology in more than 50 % of tumour cells. There was seminal vesicle as well as perineural invasion and extraprostatic extension. The surgical margin (ink stained) was positive for malignancy. IC was also observed as well as PS in the surrounding acini. Due to the rarity of prostatic SRA we performed immunohistochemistry in order to exclude the possibility of metastatic disease. PSA and P-504 s were positive CK-7, CK-20, CDX-2 and Gata-3 were negative.
Conclusion: The diagnosis of SRA of the prostate Gleason score 10 with associated IC and PS was made. The patient was treated with a combination of antiandrogens and radiotherapy. Thirty-eight months after surgery he is alive with no evidence of biochemical recurrence.

PS-25-063
Primary renal lymphoma: A case report
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Objective: The aim of this study is to review clinicopathologic findings of renal lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma), its differential diagnosis, management and prognosis.
Method: A 40-year-old woman presented with a flank pain. She had no palpable flank or abdominal masses and no lymphadenopathy. Renal sonography was normal. Pelvis computed tomography scan revealed an infiltrative mass arising from the upper pole of the left kidney and involving hilum lymph nodes. Given that renal pelvic carcinoma could not be excluded, radical nephroureterectomy was performed.
Results: Grossly the kidney contained grey ill defined solid tumour in the upper pole. Microscopy revealed a diffusely infiltrating lymphoid proliferation with small to medium sized cells, having slightly irregular nuclear contours, that expressed CD20 and Bcl-2 and was negative for CD5, Cylin-D1, CD23, CD10. The FISHi test showed no evidence of BCL2 or BCL6 gene rearrangement. Thus, the pathological diagnosis was MALT lymphoma of the kidney. Bone marrow and gastric biopsy, thoraco-abdominal CT excluded other nodal or extra-nodal location. The patient received chemotherapy, and was disease-free 14 months after surgery.
Conclusion: Primary renal MALT lymphoma is extremely rare ; it can mimic clinically other renal neoplasms, such as renal cell carcinoma. It is also important to distinguish it from other more aggressive types of renal lymphomas.

PS-25-064
Unusual testicular tumour: A case report
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Objective: The aim of this study was to describe a case of testicular plasmocytoma and discuss the differential diagnosis.
Method: A51-year-old man with medical history of multiple myeloma 4 years ago complaining of an enlarged, painless testicular mass with heterogeneous echogenicity. Testicular tumour markers were negative. Bone marrow biopsy was normal.
Results: The patient underwent radical orchidectomy. Macroscopic examination showed upper polar homogeneous whitish nodule. Histopathology demonstrated a diffuse infiltration of the testicular parenchyma by abnormal plasmocytes with varying degrees of differentiation

with positivity for CD138 and light chain restriction. Immunostaining for PLAP, c-KIT, CD20, and MPO were negatifs. The diagnosis of plasmocytoma of the testis with previous multiple myeloma in remission was retained.
Conclusion: Multiple myeloma involving the testis is rare well-documented entity. The diagnosis is confirmed by immunostaining. The differential diagnosis are lymphoma, seminoma and leukemias. This entity is a clinically and histologically diagnosed trap. Pathologist should known the patients's medical history.

PS-25-065
Pure prostatic leiomyoma: A rare case report
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Objective: Leiomyomas are benign mesenchymal smooth muscle tumours. It is common in prostate as a nodular leiomyomatosis frequently observed with benign prostate hypertrophy. However, pure leiomyoma of prostate is very rare.
Method: Here we presented a case of 77-year-old men who admitted to our hospital with complains of dysuria.
Results: The per-rectal examination, CT and ultrosound examination revealed an enlarged prostate with firm, solid nodule. The blood PSA level assessment was normal. Due to measure of prostate, open prostatectomy procedure was performed for removal of an enlarged organ. The prostate weigh was 172 gr in gross pathological examination. 50x60x60 cm in size, whitish colored and soft consistency solid nodular lesion was observed on the cut surface of the prostate. Microscopically, this nodular lesion was composed of spindle cell proliferation, without nuclear atypia, coagulation necrosis and mitotic activity. Prostatic glands were not found into the nodular lesion. Immunohistochemical evaluation showed strong intracytoplasmic positivity of desmin in the spindle cells. Accordingly, the diagnosis of true leiomyoma of the prostate was made.
Conclusion: Radiological methods are inadequate for determination of the biological nature of such nodules. Therefore, histopathology is very important for excluding of malignancy. Open prostatectomy is an effective method for both treatment and diagnostic purposes.

PS-25-066
Renal cell carcinoma (RCC) diagnosed with gastric polyp: Case report
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Objective: RCC accounts for approximately 3 % of adult malignancies. They have a strong potential to metastasize to multipl organs and one third of the patients have metastasis at the initial diagnosis. The most common sites of metastasis are liver, lung, bones and brain. Stomach metastasis is extremely rare, with 22 cases reported in the literature.
Method: A 64-year-old male was admitted to our hospital complaining of malaise and anemia. Gastrointestinal endoscopy detected multipl ulcerated polyp which the biggest one was 1,2x0,5x0,4 cm in diameter and smallest one was 0,3 cm in diameter. Microcopic examination of lesion composed of nodular and nested collection of clear cells interspersed with delicate, arborizing vasculature. The tumour were immunoreactive with antibodies raised against vimentin and CD10. The histomorphologic features and immunohistochemical finding were consistent with RCC. Two large, solid, hypervascular masses were identified in the right kidney which was confirmed by ultrasonograph (USG).
Results: The patient underwent a radical nephrectomy after gastric endoscopy and USG. The histologic examination releaved a clear cell RCC.
Conclusion: Metastasis to stomach is very rare and seems to be a late event in patients with RCC. We would like to emphasize the importance of a careful endoscopic and histopathological examination with this case

PS-25-067
Intratesticular epidermoid cyst: A rare pre-pubertal type teratoma
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Objective: To determine histological characteristics of intratesticular epidermoid cysts classified as a prepubertal type teratomas.
Method: We present the case of an intratesticular epidermoid cyst diagnosed in our pathology department.
Results: A 17-year-old man presented with painless right testicular mass. On examination, the mass was found to be firm, small-sized, with a smooth surface.On ultrasonography, this mass appeared as a heterogeneous and well-demarcated intratesticular lesion. All laboratory tests, including tumour markers, were normal.The patient underwent excision of the mass with the surrounding testicular parenchyma. An intraoperative frozen section was interpreted, and the regular pathological examination showed an intratesticular epidermoid cyst and no evidence of malignancy. Hence, the testis was spared. The final pathological examination confirmed intratesticular epidermoid cyst diagnosis by revealing a cystic lesion located in the parenchyma of the testis, containing keratinized debris .The cyst wall was composed of a fibrous epithelium, with no malignant germ cell neoplasia, no teratomatous elements or dermal adnexal structures within the cyst wall or testicular parenchyma.
Conclusion: Intratesticular epidermoid cysts are rare benign intratesticular lesions with distinctive histologic characteristics.These lesions typically occur before the age of 6 years but can be diagnosed in postpubertal age.If identified on frozen section examination, testicle-sparing surgery is performed; avoiding orchiectomy.

PS-25-069
Significance of p53-binding protein 1-nuclear expression in urothelial tumours: Implication of DNA damage response in association with tumour grades
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Objective: Recent studies suggest that genome instability (GIN) is associated with development of malignancy including urothelial carcinomas (UC). 53BP1 is a DNA-damage response molecule that accumulates in DNA double-strand breaks and is suggested to represent GIN. Our aim was to investigate the expression of 53BP1 in papillomas and UC, which had not been reported.
Method: Eight normal urotheliums, 8 urothelial papillomas, 11 low-grade UC (LGUC), and 8 high-grade UC (HGUC) were subjected to double-labelled fluorescence immunohistochemistry of 53BP1 and Ki67. Diffuse 53BP1 staining in the nucleus was determined as abnormal expression (Matsuda, 2011, Histopathology). GIN in UC was also analysed by FISH.
Results: GIN by FISH was absent in normal urotheliums and papillomas, but was 50 % and 100 % in LGUC and HGUC, respectively. Presence of abnormal 53BP1 was 0.2 % and 21.4 % in papillomas and LGUC, respectively, and distinguished LGUC from papilloma with 83.3 % sensitivity and 100 % specificity. Furthermore, co-localisation of abnormal

53BP1 and Ki67 was significantly increased in HGUC than in LGUC, distinguishing HGUC from LGUC with 62.5 % sensitivity and 91.7 % specificity.
Conclusion: 53BP1 expression analysis in UCs may represent GIN. Immunofluorescence study of 53BP1 in combination with Ki67 may be useful in diagnosing urothelial neoplasms.

PS-25-070
Foxa1 expression is a strong independent predictor of early prostate specific antigen recurrence in erg negative prostate cancers treated by radical prostatectomy
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Objective: Forkhead box protein A1 (FOXA1) is a transcription factor involved in androgen signaling with a strong relevance for lineage specific gene expression of the prostate.
Method: FOXA1 expression was analyzed by immunohistochemistry on a tissue microarray containing 11,152 prostate cancer specimens. Results were compared to important pathological and clinical parameters.
Results: FOXA1 expression was detectable in 97.6 % of 8,227 interpretable cancers and considered strong in 28.5 %, moderate in 46.2 % and weak in 22.9 % of cases. High FOXA1 expression was strongly associated with ERG expression ($p < 0.0001$). High FOXA1 expression was tightly linked to high Gleason grade, advanced pT stage and early prostate specific antigen (PSA) recurrence in ERG negative cancers ($p < 0.0001$ each). In ERG negative cancers, the prognostic role of FOXA1 expression was independent of Gleason grade, pT and pN stage, surgical margin status and preoperative PSA. Independent prognostic value became even more evident if the analysis was limited to preoperatively available features such as FOXA1 expression ($p < 0.0001$).
Conclusion: High expression of FOXA1 is an independent prognostic parameter in ERG negative prostate cancer. FOXA1 measurement might thus provide clinically useful information in prostate cancer. However, the finding subtype specific prognostic features challenges the current concept of molecular classifiers that apply to all prostate cancers.

PS-25-071
Mutations of TERT promoter and FGFR3 in urothelial carcinoma of urinary bladder in Korean patients
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Objective: TERT and FGFR3 are targets of mutation in urothelial carcinoma of bladder. The purpose of this study was to find the mutation ratio and their clinical implications in Korean patients.
Method: Direct sequencing was done. They were 70 non- urothelial carcinomas, 49 non-muscle invasive carcinomas and 64 muscle invasive urothelial carcinomas or above. They were 183 in total, male patients were 158 and female 25. The mean age was 69.9 year, and mean follow-up 52 months.
Results: Mutaion of TERT promoter was found in 39 (21.3 %), which was not associated with stage or recurrence. The mutation ratio of TERT promoter was significantly lower than that of Caucacians or Han Chinese. Mutaion of FGFR3 was found in 32 cases (17.5 %). It was more frequently found in non-invasive carcinoma than invasive carcinoma ($p < 0.01$; 95 % CI, 3.40–20.85). Disease recurrence was associated with FGFR3 mutation ($p = 0.02$; 95 % CI, 1.20–6.91), longer duration of follow-up ($p < 0.01$; 95 % CI, 1.21–1.54), and older age ($p = 0.04$; 95 % CI, 1.00–1.08).
Conclusion: The mutation ratio of TERT promoter was 21.3 % and that of FGFR3 17.5 %. FGFR3 mutation was more frequently found in non-invasive carcinoma. The disease recurrence was associated with FGFR3 mutation, longer duration of follow-up, and older age.

PS-25-072
Expression of stem related markers-Sox2 and Oct3/4 in upper tract urothelial carcinoma
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Objective: Objective of this study was to evaluate and correlate the expression of stem related markers, Sox-2 and Oct3/4, with morphological characteristics of upper tract urothelial carcinoma (UTUC).
Method: We studied 73 patients with UTUC, who had undergone open type nephroureterectomy. H&E-stained slides were used to assess histological grade, pathologic stage, growth of tumour, lymphovascular invasion, and the presence of necrosis and metaplastic changes within the tumour. Immunohistochemistry was performed to detect expression of Sox2 at dilution 1:100, and Oct3/4 at dilution 1:1000. Nuclear expression of Sox2 and Oct3/4 was considered positive. We used a 10 % cutoff point for both negative (normal) and positive (altered) specimens.
Results: Altered expression of Sox-2 was detected in 28/73 (38.4 %) of UTUC. Histologic grade, growth pattern, lymphovascular invasion, necrosis, and divergent differentiation had significant influence to expression of Sox2 in UTUC ($p < 0.001$; $p < 0.05$; $p < 0.05$; $p < 0.01$; $p < 0.0001$, respectively). Altered expression of Oct3/4 was detected in 31/73 (42.5 %), and significant association was not present with phenotypic characteristics of UTUC.
Conclusion: This investigation detected association of phenotypic characteristics of UTUC to expression of Sox2, where accumulation of this transcription factor suggested aggressive behaviour of UTUC. This influence was not detected in regard to expression of Oct3/4.

PS-25-073
Novel markers for differential diagnosis of prostate cancer and benign mimics
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Objective: The objective of this study is to assess the utility of APOD and FASN for differential diagnosis of prostate neoplasms.
Method: The radical prostatectomy specimens from 90 patients were investigated using immunohistochemical staining of APOD and FASN. The presence of high-grade prostatic intraepithelial neoplasia (HGPIN) and prostate cancer in the specimens was confirmed by a moderate to strong expression of P504S and presence (in HGPIN) or absence (in prostate carcinoma) of 34βE12.
Results: In the specimens evaluated, all carcinomas and HGPIN showed an overexpression of FASN. APOD overexpression was found to be 76 % in carcinoma and HGPIN, 7 % in HGPIN and 4 % in cancer, whereas the remaining 13 % were APOD-negative. Additionally, all benign glands were found to be APOD and FASN-negative.
Conclusion: The high incidence of APOD and FASN-positive HGPIN and prostate cancers shows the potential of these proteins as additional markers for the differential diagnosis of prostate neoplasms and benign mimickers. The reported study was supported by RFBR, research project No. 15-04-03629 a.

PS-25-074

Analysis of Notch pathway components in the tumourigenesis of testis tissue

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Objective: Testicular germ cell tumours (GCTs) constitute the most common solid tumour in men between the ages 20 and 34 years, and the incidence of testicular GCTs has been increasing in the past two decades. Intratubular germ cell neoplasi (IGCN) is defined as a pre-invasive testicular germ cell lesion and is now believed an important precursor of TGCTs. Notch receptors may have a role as an oncogene or a tumour supressor gene depending upon cell type, though the majority of studies reveal that Notch signaling promotes tumourigenesis.
Method: In the present study, we examined the expression of four Notch receptors, two ligands (Jagged1,2) and two transcription factor (Hes1,5) in normal testis (n:20), IGCN (n:20), and seminoma (n:20), tissues using immunohistochemistry, followed by scoring staining distribution and intensity.
Results: According to our results; Notch 4 expression was higher in seminoma tissues, Hes5 expression was higher in IGCN tissues compared with normal tissues. Notch 3 expression was lower in IGCN and seminoma tissues, Jagged 1 expression was lower in IGCN tissues compared with normal tissues.
Conclusion: Notch is a member of the signalling pathway that plays an important role in homeostasis and development of tissue. We explained that Notch 4 and Hes 5 overexpression and decreased levels of Notch 3 may have a role in the tumourigenesis of testis. However there is no report about the association between Notch receptors and seminoma and IGCN.

PS-25-076

Negative correlation of beta catenin expression to inflammatory response in testicular germ cell tumours

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Objective: Immune mechanisms evaluated by PD-1/PD-L1 pathway and systemic immune-inflammation index (SII) were shown to play a role in outcome in germ cell tumours (GCTs). We aimed to evaluate beta catenin expression in germ cell tumours for assessment of its possible prognostic significance for its inhibitory mechanism for tumour T-cell infiltration
Method: Surgical specimens from 247 patients with GCTs (238 with primary testicular tumour and 9 with extragonadal GCTs) were included into the translational study. Beta catenin expression was detected by immunohistochemistry, scored by the weighted histoscore (HS) method and correlated with clinicopathological characteristics, clinical outcome, PD-L1 expression and SII.
Results: Most of GCTs (86.2 %) showed a beta catenin expression. Seminoma exhibited significantly lower expression compared to non-seminoma GCTs. High beta catenin expression was associated with primary mediastinal non-seminoma tumours, intermediate/poor risk disease and highly elevated tumour markers. Beta catenin showed a positive correlation with the PD-L1 in tumour, but not on TILs and an inverse correlation with SII. Survival analysis with the Kaplan-Meier method did not show differences in PFS and OS.
Conclusion: The present work demonstrated association of βcatenin expressions in GCTs with clinical characteristics, PD-L1 and SII. Our data imply that WNTbeta catenin signalling may comply with differences among seminomas and non-seminomas and is associated with systemic inflammation and GCTs expressing PD-L1. Supported by APVV-0016-11.

PS-25-078

Methods of atomic-force microscopy within the scope of research of oncological processes

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Objective: Atomic-force microscopy (AFM) becomes one of the innovational methods, which allows to make first steps in nanopathology of oncological processes.
Method: AFM was performed in laboratory «Ntegra-Aura» with usage of software «NOVA» and «ImageAnalysis». The researches of tissues of 20 patients with prostate cancer, 25 patients with kidney cancer and 15 patients with urine bladder cancer were performed.
Results: The deformed glands with branched forms, consisted of atypical polymorphic cells with weak connection between them, were detected at research of prostate cancer. The branched structures, consisted of one or dozens cells, sprouted into tissue, were detected at kidney cancer and urine bladder cancer. It was revealed, that contacts between cells were 0,45 ± 0,10 μm and 3,85 ± 0,40 μm in separate sites at rapid progression of disease (0,25 ± 0,05 μm at slow progression), what exceeded sizes of tumour cells.
Conclusion: The usage of AFM in research of native tissues as well as fixed samples, allows to perform this method for express diagnosis in clinic and to research of morphogenesis of tumour's growth on nanostructure level.

PS-25-079

Immunohistochemical study of molecular subtypes in muscle-invasive bladder cancers: Our experience in the first year since the new WHO recommendation

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Objective: To analyze the molecular subtype of the muscle-invasive bladder cancers (MIBCs) diagnosed for 14 months and assess the possible impact on the patient's prognosis
Method: We performed immunohistochemical study with 4 markers (CD44, KRT20, KRT5/6 and p53) to all MIBCs (19 cases). We determined the molecular subtype and divided them into luminal, basal, p53-like, luminal/p53-like, basal/p53-like and non-conclusive. Epidemiological (age, sex, smoking, tumour location and measurement) and clinical aspects (stage, treatment and follow-up) were collected
Results: 18/19 men (94.7 %), 1/19 women (5.3 %) Mean age: 71.8 years. We obtained 2 luminal (10.5 %), 2 basal (10.5 %), 3 p53-like (15.8 %), 4 luminal/p53-like (21 %), 4 basal/p53-like, 3 non-conclusive (15.8 %) and 1 mixed (5.3 %) Clinical information and follow-up were obtained in 12/19 patients (63.16 %): stage II (33.33 %) (2 luminal/p53-like, 1 luminal, 1 p53-like); 2 stage III (16.67 %) (1 basal, 1 basal/p53-like); and 6 stage IV (50 %) (2 inconclusive, 1 luminal, 1 basal, 1 p53-like, 1 basal/p53-like) 2 patients died
Conclusion: We have not yet been able to verify the effect of the molecular subtype on the prognosis of the patient due to the short time of follow-up. According to studies, other immunohistochemical markers might be more useful in determining the molecular subtype, among which GATA3, uroplakin or KRT14. Probably, by expanding the immunohistochemical panel, we will be able to subclassify a greater number of cases

PS-25-080

Expression of stemness markers Oct3/4 and Nanog in early invasive T1 urothelial bladder cancer

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Objective: To assess the significance and prognostic impact of putative cancer stem cell markers Oct3/4 and Nanog in early invasive urothelial bladder cancer (UBC).
Method: Immunohistochemical analysis of Oct3/4 and Nanog expression comprised specimens from 298 patients with T1 UBC, included in tissue microarrays. Expression status was correlated with clinicopathological and follow-up data.
Results: Intense nuclear Oct3/4 expression was found in 47 % of the tumours, moderate in 21.8 %, and low/absent in 31.2 %. Nanog stained nuclei (41.3 %), with low to intermediate intensity in all positive cases, both nuclei and cytoplasm, or only cytoplasm. Oct3/4 correlated with nuclear Nanog expression ($p < 0.001$), while Nanog nuclear and cytoplasmic positivity exhibited inverse correlation ($p = 0.019$). Neither Oct-3/4, nor Nanog nuclear expression was significantly associated with tumour grade, morphology, and recurrence. Nanog cytoplasmic expression (strong intensity observed in 51 cases) was associated with high grade, male gender, cancer specific death ($p < 0.001$, $p = 0.006$, and $p = 0.002$, respectively), and, in Kaplan-Meier analysis, with worse survival of UBC patients ($p = 0.002$). In Cox regression analysis, high grade, strong Oct3/4, and Nanog cytoplasmic expression were independent predictors of poor prognosis ($p < 0.001$, $p = 0.028$, and $p = 0.039$, respectively).
Conclusion: Expression of stemness markers Oct3/4 and Nanog has prognostic significance, with potential to improve therapy decision-making in early invasive T1 UBC.

PS-25-081
Growth pattern proportion and Ki-67 index of primary renal well-differentiated neuroendocrine tumour
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Objective: Primary renal well-differentiated neuroendocrine tumour (WDNET) is extremely rare and parameters to predict its prognosis at diagnosis are not available.
Method: Five cases of renal WDNET were collected. After reviewing slides, the proportions of each growth patterns were determined. PHH-3 and Ki-67 immunostaining with morphometric analysis were carried out.
Results: One of five cases showed lymph node and liver metastasis, another showed lymph node metastasis only. The remaining three did not show metastasis. Histopathologically, renal WDNETs mainly composed of ribbon-like and sheet-like growth pattern. The proportions of sheet-like pattern were 75 % in the case with liver metastasis and 7 % in the case with lymph node metastasis only. The remaining three cases mainly contained ribbon-like patterns. Ki-67 index was 8.27 % in the case with liver metastasis and 3.30 % in the case with lymph node metastasis only. Ki-67 index of the remaining three cases were 1.24 , 0.60 , and 0.52 %. We could not clearly identify any mitotic figures or PHH3-positive cells in all cases.
Conclusion: Two out of the five WDNETs showed aggressive behavior, which showed higher proportions of sheet-like pattern and higher Ki-67 indexes. These results suggested that the sheet-like patterns and high Ki-67 indexes could be markers for predicting aggressiveness of renal WDNET.

PS-25-082
Von Hippel Lindau protein expression in embryonal carcinoma and yolk sac tumour
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Objective: The VHL protein (pVHL) is encoded by the von Hippel Lindau tumour suppressor gene and it plays a key part in cellular oxygen sensing by inactivating hypoxia-inducible factors. Loss of the pVHL due to mutation of the VHL gene leads to downstream activation of genes that promote tumourigenesis.
Method: We studied the immunohistochemical expression of the pVHL (clone SC5575, Santa Cruz, CA) in 7 paraffin block mixed germ cell tumour cases, 5 of testicular and 2 of mediastinal origin, composed mainly by embryonal carcinoma and yolk sac tumour. Embryonal carcinoma areas were immunophenotypically CD30+, SALL4+, OCT3/4+ while yolk sac areas were aFP+, Glypican-3+, SALL4+, OCT3/4-.
Results: All embryonal carcinoma cases were positive for pVHL protein with strong cytoplasmic expression. We performed double staining (nuclear-OCT3/4 and cytoplasmic-pVHL) to highlight the concurrent expression of the two proteins in embryonal carcinoma. Accordingly 6/7 cases of yolk sac tumour were at least focally pVHL positive as demonstrated by the OCT3/4 negative - pVHL positive tumour cells.
Conclusion: pVHL is mainly expressed in renal cell carcinoma, ovarian clear cell carcinoma and cholangiocarcinoma. We demonstrate the expression of the pVHL in embryonal carcinoma and yolk sac germ cell tumours.

PS-25-083
GATA-3 and CK5/6 as potential markers of intrinsic molecular subtypes of urinary bladder carcinoma
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Objective: Genome expression profiling of urinary bladder carcinoma has shown two intrinsic molecular subtypes (luminal and basal) and a small group of double-negative tumours. A recent publication, based on image analysis, argues that GATA-3 and CK5/6 evaluation could be enough to identify these subtypes. We have evaluated GATA-3 and CK5/6 immunostaining patterns in bladder urothelial carcinoma.
Method: We used two tissue microarrays to asses GATA-3 and CK5/6 immunohistochemical expression in 64 muscle-invasive bladder urothelial carcinoma samples (22 of them with squamous differentiation) corresponding to transurethral resection.
Results: Four immunohistochemical patterns were identified according to immunostaining extent and intensity for both GATA-3 and CK5/6. Staining patterns with intense and diffuse positivity for both markers were mutually exclusive. In addition, seven double-negative cases were identified while the rest showed combined patterns. The presence of squamous differentiation was not always correlated with CK5/6 expression.
Conclusion: Intense and diffuse positivity for either GATA-3 or CK5/6 allows to define two mutually exclusive urothelial carcinoma groups that could correspond to the luminal and basal subtypes, respectively. However, there are equivocal cases with dual positivities. On the other hand, the role of squamous differentiation is still to be completely elucidated.

PS-25-084
Concordance of histologic variants of urothelial carcinoma between transurethral resection and radical cystectomy
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Objective: Urothelial carcinoma (UC) is a heterogeneous disease, reporting variant histology (VH) is recommended because of prognostic and therapeutic implications. We evaluated the concordance of HV of UC between transurethral resection of bladder (TURB) and radical cystectomies (RC).

Method: One hundred and ten patients, who underwent RC from 1997 and 2013 were included. The presence of HV of UC in TURB/RC was assessed according to the 2016 WHO classification.
Results: Amongst 110 patients, 68 (62 %) were diagnosed with one VH, 42 (38 %) had multiple patterns. Squamous differentiation (17 % TURBT, 18 % RC) was the most common single VH, followed by micropapillary (9 % TURBT , 12 % RC), 21 UC (19 %) showed discordance of VH between TURB and RC, in non métastatic cases ($n = 66$) discrepancies were seen in 8 cases (12.1 %), in metastatic cases ($n = 44$) in 13 (29.5 %). Most differences were between squamous and sarcomatoid ($n = 4$), and microcystic and nested ($n = 4$) VH.
Conclusion: Squamous and micropapillary VH were the most frequent VH. Difficulties in distinguishing squamous versus sarcomatoid and microcystic versus nested because of overlapping features were encountered. Metastatic UC display more discrepancies between initial diagnosis and RC. These findings have to be taken into consideration, when treating patients, especially if administering neoadjuvant chemotherapy.

PS-25-085
Neuroendocrine carcinoma of the urinary bladder. A unit's experience over 7 years
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Objective: Neuroendocrine carcinoma (NEC) of the urinary bladder is a rare entity, accounting less than 1 % of urinary bladder malignancies. We present our experiences with 11 patients diagnosed with bladder NEC in our hospital, 4 with large cell NEC and 7 with small cell NEC.
Method: This is a retrospective study including patients diagnosed with bladder NEC between March 2010 and March 2017 at our hospital. Demographic data, clinical presentation, histologic and immunohistochemical findings, as well as treatments and survival were collected and analyzed.
Results: Over 7 years, 11 patients with a median age of 76 years were diagnosed with bladder NEC; 4 of them were large cell NEC and 7 small cell NEC (1 female). There were included four mixed neoplasms, three associated with urothelial carcinoma and one with epidermoid carcinoma. After bladder transurethral resection (TUR) and histological diagnosis, 64 % (7 patients) were treated with radical cystectomy, some of them received aditional chemoterapy; the remainder were treated with chemotherapy or paliative treatment.
Conclusion: NEC of the urinary bladder is a rare and aggressive entity commonly diagnosed in elderly males and frequently with advanced disease stage. Overlapping histological features and immunophenotype between small cell NEC, large cell NEC and mixed neoplasms difficult an appropriate management of them. A clinical database for NEC of the urinary bladder and prospective studies are needed in order to establish and verify the best treatment for this malignancy.

PS-25-086
Evaluation of understating and residual tumour after a re-resection for bladder cancer
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Objective: Cancer understating and residual tumour after transurethral resection (TUR) are the most important factors for recurrence, while absence of detrusor muscle in TUR is the most important factor for understating. We aim to assess understating and residual tumour rates after TUR.

Method: Patients were prospectively enrolled in our Re-Resection (Re-TUR) study protocol. The Re-TUR was performed when no muscle was found in the sample, in T1 tumours and high-grade tumours.
Results: We included 86 Re-TUR. 19 (22.1 %) patients did not have detrusor muscle in the first TUR. Stages requiring Re-TUR were: TaG I-II in 5 cases (5.8 %), T1GII in 33 (38.4 %), T1GII + CIS in 4 (4.7 %), T1GIII in 31 (36 %), T1GIII + CIS in 13 (15.1 %). Staging after Re-TUR was: pT0 66 cases (76.7 %) Tis in 6 cases (7 %), TaGII-III in 3 (3.5 %); T1GII-III in 10 (11.6 %) and T2GIII in 1 (1.2 %). We found 19 residual tumours, 6 of them CIS previously diagnosed and 13 (15.1 %) true residual tumours. We only had 1 case of understating of the specimen (1.2 %).
Conclusion: T1GII and GIII (High grade ISUP-2004) features were the only cancers with real danger of residual tumour and understating -and therefore worthy to perform Re-TUR.

PS-25-087
Morphologic variability in t(6;11) translocation renal cell carcinoma: Analysis of 9 cases
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Objective: t(6;11) translocation renal cell carcinomas (tTRCCs) are mostly characterized by biphasic morphology. Tumours are composed of large eosinophilic cells and small pseudorosettes surrounded by small lymphocyte-like cells. However, several different patterns were described in the literature recently.
Method: Nine cases of tTRCC were selected of 38 translocation carcinomas in our registry. Cases were examined using immunohistochemistry and FISH. Morphologic pattern was analyzed in detail.
Results: Information about the patients was available in 8/9 cases. Patients were 3 males, 5 females, age range 14-77 years. Size of the tumours (known in 7/9 cases) ranged from 3 to 14 cm. Eight cases followed benign clinical course, one tTRCC had aggressive behavior. All cases were immunoreactive for HMB45 and variably for cytokeratins. FISH confirmed translocation of TFEB in all 9 cases. 5/9 cases had classic biphasic morphology. In 3/9 cases, pseudorosettes were sparse and inconspicuous. One case mimicked eosinophilic solid and cystic renal cell carcinoma described recently. One aggressive case had typical tTRCC morphology.
Conclusion: tTRCC have more variable morphology, than it was originally estimated. Diagnosis of tTRCC should be considered even in tumours with atypical morphology.

PS-25-090
Phosphodiesterase 4b expression in a canine experimental model of prostatic hyperplasia
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Objective: To assess if prostatic hyperplasia (PH) induces changes in the expression of phosphodiesterase (PDE) 4b in a canine model of induced PH.
Method: An experimental group of 5 Beagle dogs were surgically castrated and administered 25 mg of 5α-androstane and 0.25 mg of 17β-estradiol 3 times/week during 30 weeks. Three controls were treated with placebo. Biopsies were taken before first treatment and in the 6th, 24th and 36th week. PDE4b expression histoscore was assessed in prostatic epithelium, stroma and blood vessels. Statistical differences were evaluated using the U Mann-Whitney test.
Results: No changes in stromal and blood vessel PDE4b expression were found. Epithelial expression of PDE4b increased along the experimental stages and was higher in glands around inflamed areas. Histoscore results in cases and controls are summarized in table 1.

Conclusion: In this canine experimental model, induced PH is associated to progressively increasing PDE4b expression in epithelial cells, in contrast with the bimodal increase in the controls. These results indicate that PDE4b deserves further investigation in human PH. FIS/CarlosIII/FEDER/PI15/00452, Spanish Ministry of Health.

PS-25-091

Expression of erythropoietin and neuroendocrine markers in clear cell renal cell carcinoma (CCRCC)

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Objective: To investigate the expression of erythropoietin (EPO) and neuroendocrine markers in clear cell renal cell carcinoma (CCRCC).
Method: The medical records from 44 patients treated with partial or radical nephrectomy at St. Olavs Hospital – Trondheim University Hospital between 2010 and 2016 were retrospectively reviewed and the corresponding specimens re-evaluated and further sub-classified into CCRCC or non-CCRCC. Immunohistochemical staining with antibodies against EPO and neuroendocrine markers was performed.
Results: The 33 patients who were diagnosed with CCRCC had 35 tumours, where 34 tumours were CCRCC and one tumour was papillary adenoma. Of the 11 patients diagnosed with non-CCRCC seven were papillary renal cell carcinoma (PRCC) type 1, two were PRCC type 2, and two were chromophobe renal cell carcinoma. Of the CCRCC 33/34 (97 %) were positive for EPO, and the same 33 (97 %) tumours expressed NSE. Two of 34 (6 %) CCRCC had focal expression for synaptophysin, and three of 34 (9 %) CCRCC were positive for CD56. EPO and NSE were negative in all non-CCRCC, and CgA was negative in all tumours examined.
Conclusion: In summary, we found that the majority of tumours examined with morphology consistent with CCRCC demonstrated strong expression for EPO and NSE, whereas the same markers were negative in non-CCRCC. The above findings suggest that there is a strong link between CCRCC and the expression of EPO and NSE.

PS-25-092

Study of status of CD10, e-cadherin and β-catenin immunohistochemical staining in urothelial bladder carcinoma (UCC) before and after intracystic infusion therapy

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Objective: Our goal is to record and evaluate the status of CD10, e-cadherin, β-catenin immunohistochemical staining in UCC before and after therapy. Our sample constitutes of 24 patients with UCC divided in four groups according to tumour grade: 12 in group A (low grade before and after), 1 in group B (high grade before and after), 4 in group C (low grade before, high grade after), 7 in group D (high grade before, low grade after)
Method: Immunohistochemistry was performed on paraffin embedded tissue. CD10 membrane immunoexpression was evaluated qualitative (scale 0–3), e-cadherin and β-catenin both qualitative (scale 0–3) and quantitative (% positive expression)
Results: As far as it concerns CD10, minor alterations were observed in group C and major in group D (3/4 became negative). E-cadherin status was virtually invariable. More statistically significant alterations were observed in β-catenin: group A (in 4/12 there was a raise), group B (raise), group C (invariable), group D (in 1/7 a decrease, in 2/7 an increase)
Conclusion: UCC relapses frequently after therapy and more studies and researches need to be performed in order to come to stable conclusions concerning how immunohistochemical pathological studies can help clinicians to treat their patients in the most effective way

PS-25-096

Neuroendocrine differentiation in hormonally treated prostate cancers

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Objective: The neuroendocrine differentiation (NE) in prostate carcinoma continues to be a topic of great interest, particularly viewed from the perspective of NE carcinomas developed in hormonally treated conventional prostate adenocarcinoma.
Method: Cases of prostate NE carcinomas, secondary to hormonal treatment, diagnosed between 2010 and 2016 were selected from the Department of Pathology database. The cases of prostate adenocarcinoma with focal NE differentiation and prostate NE carcinomas of untreated patients were excluded. The following immunohistochemical (IHC) makers were used for establishing the diagnosis: CgA, Syn, PSA, Prostein, PSMA, TTF1, Ki67, CK7, CK20.
Results: In the mentioned period there were 4 cases of prostate NE carcinomas secondary to androgen deprivation therapy diagnosed in patients aged between 62 and 81 years. The original tumours had Gleason score between 7 and 10. In two of the 4 cases, the NE small cell carcinoma was associated to conventional adenocarcinoma in the TUR-P specimen, while in the other two cases, the NE differentiation was detected in the liver metastases as small cell NE carcinoma.
Conclusion: The NE differentiation should be considered in the progression of hormonally treated prostate conventional adenocarcinomas and IHC documented. The hormonally treated prostate adenocarcinomas can be the starting point for visceral metastases with small cells NE carcinoma appearance.

PS-25-097

A study on the expression of ITGA5 on clear cell renal cell carcinoma (CCRCC)

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Objective: Clear cell renal cell carcinoma (ccRCC) is the most frequent and aggressive renal cancer. We need more accurate prognostic and predictive factors than clinic-pathological staging. Some hypotheses postulate that the presence of genes involved in the epithelial-mesenchymal transition, such as integrin subunit alpha 5 (ITGA5), could be related to prognosis. We aimed to look into the association of ITGA5 expression with ccRCC prognosis.
Method: We analyzed the expression of ITGA5 by immunohistochemistry in a tissue microarray of 46 ccRCC (one patient Fuhrman 1, 14 Fuhrman 2, 18 Fuhrman 3 and 13 Fuhrman 4), stage pT3. Clinical follow-up was also assessed.
Results: Only four tumours showed positivity for ITGA5. Of those, two patients died of disease, having a shorter survival time (25,60 and 30,17 months) than those without expression of ITGA5 (13 patients, with a median survival time of 53,35 months). Furthermore, when tumours with the same Fuhrman grade and presence of necrosis were compared, still those with ITGA5 expression showed worse prognosis.

Conclusion: ITGA5 has been associated with a poorer prognosis in ccRCC, as seen in our series, although these results are limited because of the low number of cases examined. Further studies need to be undertaken.

PS-25-098

Impact of the expression of epithelial-mesenchymal transition markers in renal cancer: A study on the expression of PLAUR on clear cell renal cell carcinoma (CCRCC)

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Objective: New molecular and immunohistochemical markers are been studied to achieve a better understanding of the clinical course of clear cell renal cell carcinoma (ccRCC). An analysis of Plasminogen Activator Urokinase Receptor (PLAUR) expression and its relationship to prognosis in ccRCC was performed.
Method: We analyzed the expression of PLAUR by immunohistochemistry in a tissue microarray of 46 ccRCC (one patient Fuhrman 1, 14 Fuhrman 2, 18 Fuhrman 3 and 13 Fuhrman 4), stage pT3, as well as the clinical follow-up.
Results: Only two tumours were positive for PLAUR. Both of them had a Fuhrman grade 3 and died of disease, having a shorter survival time (16.62 months) than the other patients with tumours Fuhrman grade 3 that died of disease (four patients), having a shorter survival time (68.43 months).
Conclusion: PLAUR, a protein involved in the epithelial-mesenchymal transition, has been postulated to be associated with adverse prognosis in renal cancer. Although a poorer survival was observed, we have only seen two positive cases in our series. Based on these results, we believe PLAUR deserves more extensive study as a prognostic factor.

PS-25-099

Enhancing the efficacy of the fusion guided biopsy approach for prostate cancer

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Objective: Recent softwares that make it possible to combine high-resolution magnetic images with real-time ultrasound images, seem to increase the success of detecting prostate cancer radiologically. Nowadays, active surveillance is the preferred method for the patients with low risk prostate cancer patients who will have indolent disease that will not need to be treated radically.
Method: We newly started to implement fusion biopsy technique at our center and performed 37 prostat fusion biopsies by this time.
Results: We diagnosed 15 adenocarcinomas of 37 lesions which were classified according to PI-RADS, and the rest 22 were benign prostate tissues. We believe a detailed histopathological description of the lesions included in the PI-RADS classification, will increase the success of the fusion biopsy technique, which is becoming radiologically the current practice.
Conclusion: As is well known, diagnosing the prostate cancer is not enough itself, but it is also a necessary to find out low-risk disease at the same time. A detailed histopathological description of any benign lesion, and accurate analysis of patterns and gleason scoring of adenocarcinomas classified according to PI-RADS, has central utility in improving the success of fusion biopsy technique.

PS-25-100

Prostatic leiomyosarcoma as an unusual diagnosis for acute urinary retention: A case report

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Objective: Prostatic leiomyosarcoma is a rare (less than 0,1 % of primary prostate malignancies) and very aggressive neoplasm, with poor outcome. We will report a case.
Method: An 87-year-old male, with history of mantle cell lymphoma treated with cyclophosphamide, presented in the Emergency Department with acute urinary retention (AUR) complaints. Physical examination and ultrasound findings confirmed an enlarged and heterogeneous prostate. Serum PSA value was within normal limits. The patient was treated with the clinical hypothesis of benign prostatic hyperplasia and a transvesical open prostatectomy was performed
Results: The histopathological examination identified a proliferation of spindle cells, with moderate nuclear pleomorphism and necrosis. Imunohistochemical analysis (Smooth Muscle Actin and Desmin positive; S-100, CD117, CD34 and Beta Catenin negative) supported the final diagnosis: prostatic leiomyosarcoma.
Conclusion: Our case has some important educational messages: leiomyosarcoma is a highly fast-growing tumour, enhancing the pathologist role in establishing the diagnosis, mainly because differential diagnosis of AUR are extensive (of which leiomyosarcoma is not among the most common causes) and prognosis is dependent on acting quickly and decisively. Although there are reports of leiomyosarcomas following cyclophosphamide therapy, mostly of the urinary bladder, the low doses received by our patient seem to exclude a causal relationship.

PS-25-101

On integrative pathology on example of radiogenic urinary bladder (UB)

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Objective: Vesical pathology is essential for whole organisms - cystitis can cause pyelonephritis followed by renal hypertension. Model for multidimensional & holistic, i.e. functional&morphological investigations of radiocystitis is given.
Method: UB-motor/electrical activities: X-/gamma-radiation = XR, microscopy
Results: I.-Patients. (Cystotonometry, $n = 150$). Vesical-pressure, micturition, urothelial-potentials are changed 1–12 months after oncological radiotherapy (Gamma-/X-rays70Gy). II.-Pathophysiology. XR induce tonic-contractions in detrusor: Human = H (>1Gy, surgical-tissue)/guinea-pig = GP/rat (>10–50 Gy), increase of spontaneous-phasic/SPC = 4.04 ± 0.75/min, decrease of tonic-contractions of trigonum/STC = 0.28 ± 0.15/min. Negative chronotropic effect. SPC/STC appear also in UB in-toto/in-vitro et in-vivo ($n = 420, p < 0.01$). Detrusor-myocytes (intracellular-rec, $n = 120, p < 0.01$): After stretch (3–80 mN) appear electrical-spike-transformation (63.29 ± 4.96/min) into burst-plateaus (1.54 ± 1.18/min) augmentation rate of spikes-rise (RR: 0.41 ± 0.19/3.27 ± 0.76 V/sec) & -fall (RF 0.43 ± 0.28/2.32 ± 0.58 V/sec resp), caused by mechanosensitive ionic-channels. No information about radiogenic-effects. III.-Pathomorphology. After local XR of UB in vivo/rats (2–6 weeks) appear histologically hyperemia, lymphocyte-infiltration, interstitial-fibrosis. Ultra-structure (electron microscopy) demonstrate essential differences between H-&GP-detrusor. IV.-Comparative observations. Various differences in pathophysiological/-morphological radiogenic effects are observed in detrusor, pyeloureter, vas-deferens/H-GP.

Conclusion: Similar models for an integrative pathology (I.-IV.) about immediate/acute/chronic radiogenic effects on different level (patient to cellular-molecular) can permit better analysis of pathogenesis, e.g. radiocystitis supporting more effective therapy-prophylaxis of bladder hypertonia, incontinence,etc.

PS-25-102

Urinary bladder hamartoma: A unique case with diagnostic pitfalls

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Objective: Bladder hamartoma is a very rare benign tumour only fourteen cases reported in the literature to date. Bladder hamartoma may be accompanied by syndromes or may be isolated. It may be present hematuria, abdominal pain, renal pain, pollakiuria, urinary voiding symptoms, it may be diagnosed incidentally. One third of the cases are localized in the posterior wall. Definitive diagnosis is by pathological examination.
Method: Herein we present a case and brief review of literature of a rare tumour in a 50-year-old male patient with bladder hamartoma.
Results: The patient was a 50-year-old man presented with hematuria and bilateral side pain. Ultrasonography disclosed increased wall thickness, measuring 48x8 mm, located on the posterior wall of bladder. CT scan showed increased asymmetric wall thickness at the side of entrance of ureters on the porterior wall of the bladder and and approximately 2.5 mm in diameter with a hyperdense stone on the adjacent left ureteral orifice
Conclusion: Transurethral resection (TUR) was performed. Microscopically polypoid tissue composed of tubuloglandular structures, nested bening urothelial epithelium, variety of stromal components was seen. In the sub-epithelial stroma, round to oval-shaped von Brunn's nests were visible . The stroma surrounding these nests had a spindle shaped cells. Some gland had intestinal metaplasia. Considering clinical, radiological and most important pathologic findings, this case defined as bladder hamartomas. Top differential diagnosis of bladder hamartomas are cystitis glandularis and embryonel rhabdomyosarcoma. Although an exceptionally rare finding, this case has added the bladder hamartoma as another point to the ever expanding list of possible causes of urinary symptoms.

PS-25-103

Clear cell adenocarcinoma of the bladder associated with endosalpingiosis and papillary urothelial carcinoma

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Objective: We report the case of a 48 years old female patient who was admitted in the hospital for hematuria. On cystoscopy and CT exam, an infiltrating bladder tumour is revealed. Therefore anterior pelvectomy with lymphadenectomy is performed.
Method: The surgical specimen is sent to pathology for processing and examination using the classical method. CK7, CA-125, p53 and Ki-67 immunohistochemical markers were used.
Results: Grossly, the bladder presents an ulcerated whitish-grey tumour of 4/2 cm with ulceration and necrosis infiltrating the bladder wall. On microscopic examination, the tumour consists in clear cell adenocarcinoma infiltrating the detrusor muscle with negative lymph nodes. Also, mullerian remnants (endosalpingiosis) are present in the bladder wall and, adjacent to the tumour, a small area of pT1 low-grade papillary urothelial carcinoma is observed. The uterus and ovaries are not involved by the tumoural process. Tumour cells were positive for CK7, CA-125 and p53, with a high Ki-67 index.
Conclusion: Primary clear cell adenocarcinoma of the bladder is a rare diagnosis with less than 50 cases reported in the literature. The tumour might be associated with mullerian remnants and urothelial carcinoma. Before making this diagnosis in a female patient, the origin in the female genital tract must be excluded.

PS-25-104

A rare case of adult cystic rete testis dysplasia

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Objective: Cystic rete testis dysplasia is a rare lesion, characteristically development in origin and typically presenting in the paediatric population; being strongly associated with ipsilateral renal agenesis and renal dysplasia. Cases in adulthood are exceptionally rare.
Method: Herein we present a case of cystic rete testis dysplasia occurring in a 56-year old adult male, without associated renal anomalies.
Results: The patient presented with slowly progressive left testicular pain and swelling. In view of a clinical suspicion of epididymo-orchitis, he was started on broad spectrum antibiotics, however, he did not improve. An ultrasound of the testicle showed a complex intratesticular mass, suspicious for tumour. Serum tumour marker levels were normal. A left radical orchidectomy was thus performed. On sectioning of the testicle, a 6 cm multiloculated cyst containing haemorrhagic fluid was found within the testicle. Histologically, the cyst communicated with the rete testis, was lined by a uniform flattened ciliated cuboidal epithelium and was surrounded by a smooth muscle layer. Subsequent radiological assessment of the renal tract did not show any anomalies.
Conclusion: This unique case presents a unique clinical manifestation of an exceptionally rare adult testicular malformation. Only a single case of adulthood cystic rete testis dysplasia has been recorded, presenting as an inguinal hernia.

PS-25-106

GATA3 a useful marker of seminal vesicle epithelium

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Objective: We have observed a positive inmunohistochemistry (IHC) for GATA3 in seminal vesicle with a masive infiltration of bladder urothelial carcinoma.
Method: To formally investigate this issue, seminal vesicle sections coming from six cistoprostatectomies with urothelial carcinoma infiltrating the prostate and seven prostatectomies with acinar adenocarcinoma of the prostate were evaluated, in our institution, by IHC for GATA3.
Results: GATA3 was positive in 92 % of seminal vesicles, in 77 % of basal and epithelial cells of the prostate an in 7 % of acinar adenocarcinoma of the prostate.
Conclusion: GATA3 is useful as a seminal vesicle epithelial marker, besides the positivity in urothelial carcinoma, breast and pancreatobiliar epithelium.

PS-25-107

Mixed epithelial stromal tumour of the kidney (MEST): A case report

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Objective: MEST is a benign tumour composed of epithelial and stromal cells, mainly observed in perimenopausal women, most showing benign course and rarely associated with aggressive behavior.

Method: A 34yo woman presented with pain and a palpable mass in her right kidney. Radiological studies showed a lesion compatible with cystic renal cell carcinoma (RCC). Right nephrectomy was performed. Macroscopic examination revealed a well circumscribed, multicystic tumour measuring 11,5X10,5X8cm, with solid septa of thickness up to 0,8 cm.
Results: Microscopically the tumour was composed of cystic and stromal component The former included cysts and tubules lined by benign cuboidal to hobnail epithelium. The stromal component, situated in the septa, had variable cellularity, including collagenous areas, fibroblasts and smooth muscle cells. No nuclear atypia or mitoses were present. Epithelial cells were positive for RCC, CK7, CK34βE12, CK19, AMACR and CK8/18, while the stroma expressed positivity for SMA, PgR, CD10, InhibinA, Desmin and calretinin.
Conclusion: A differential diagnosis of multilocular cystic renal neoplasm of low malignant potential, tubulocystic RCC, clear cell papillary RCC, adult cystic nephroma and MEST was discussed. Recognition of a stromal component, the immunohistochemical findings and the absence of desmoplastic reaction of the stroma or cellular atypia were compatible with the diagnosis of MEST.

PS-25-109
Fatal evolution of a case of emphysematous cystitis
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Objective: Emphysematous cystitis, a rare urinary tract infection commonly caused by E.coli, K.pneumoniae and mainly associated with diabetes mellitus, is characterized by the presence of gas within the bladder wall.
Method: A 65 year-old diabetic man was admitted to the Surgery Department for diffuse abdominal pain and ultrasonographic findings consistent with common bile duct obstruction, the clinical course being rapidly complicated by severe inflammatory response syndrome and acute kidney failure. Open cholecystectomy revealed multiple pelvic abdominal adhesions and a necrotic, emphysematous appearance of the urinary bladder. CT scan showed pelvic pneumoperitonitis and gas within the anterior abdominal wall and scrotum. Cystectomy and bilateral ureterostomy were performed in the Urology Department. The patient died 1 day later.
Results: Grossly, the cystectomy specimen presented a large perforation (3.5 cm diameter) with ragged edges on the anterior wall and necrotic tissue covering the whole cavity. Microscopically, adjacent to the perforation, the normal histologic architecture was replaced by a necrotic mass; on the posterior wall, patchy necrosis was identified between areas of mucosal degeneration and ulceration, acute inflammatory infiltrate in muscularis propria and gas-filled vesicles.
Conclusion: The severity of morphological lesions, leading to a fatal evolution, is the key element of this unique case.

PS-25-110
Relation of prostate adenocarcinoma neuroendocrine differentiation to Gleason system
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Objective: The present study aimed to test any existing relation between the extent of neuroendocrine differentiation and the histological grading of prostate adenocarcinoma, as expressed through the Gleason scoring system.
Method: Needle biopsy samples were obtained from 43 patients and histological diagnosis (including Gleason score assessment) was followed by immunohistochemistry testing of chromogranin A (chrA), neuron-specific enolase (NSE), and Ki-67 expression. ChrA reactivity was scored both according to di SantAgnese and by dividing patients into three categories: <10 %, 10–20 %, and >20 % chrA-positive tumour cells. We used a similar score for tumour NSE expression, with thresholds at 33 and 66 % NSE-expressing cells.
Results: Results show that chrA and NSE expression can be related to Gleason scores when using two patient groups, ie harbouring high- (Gleason 6 and 7) and low-differentiation (Gleason 8 and 9) adenocarcinoma. Thus, we found a higher probability of low-differentiation tumour diagnosis if di SantAgnese scores were high (++ and +++) or if >33 % of cells were NSE-positive. Conversely, low neuroendocrine scores are associated to a higher probability of finding a well-differentiated tumour.
Conclusion: Our data suggest that neuroendocrine differentiation is inversely related to histological differentiation of prostate adenocarcinoma.

PS-25-111
Uncommon case of familial Sertoli cell tumour of the testis
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Objective: Sertoli cell tumours (SCT) are uncommon neoplasms of the testis, therefore the diagnosis, classification, and treatment of these tumours pose a real challenge for both urologists and pathologists. We report a case of testicular SCT, diagnosed in two brothers, 11 years apart.
Method: In 2002, the first patient, 20 years old, underwent left orchiectomy for a testicular tumour. In 2013, his 35 years old brother, also lacking significant medical history or elevated levels of serum markers (ßHCG, AFP, LDH), was admitted to the same Urology Clinic. A testicular tumour was suspected and he underwent tumourectomy. Both testicular tumours were investigated using an immunohistochemical panel: calretinin, WT1, inhibin, CK, vimentin, EMA, S100, PLAP, CD117, ß-catenin.
Results: In the first case, the gross examination revealed two whitish tumour masses in the testicular parenchyma, 1.5 and 1.8 cm in diameter. In the second case, a single tumour mass of 1.1 cm in diameter was found in the testis. Microscopic diagnosis of large-cell calcifying Sertoli cell tumour of the testis in the former case and Sertoli cell tumour—NOS, in the latter, was made.
Conclusion: The presented cases are unique, as the two Sertoli cell tumour subtypes, in the two brothers, developed apparently in the absence of any evidence of genetical syndrome.

PS-25-112
Inflammatory myofibroblastic tumour arising in the adrenal gland: A case report
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Objective: Inflammatory myofibroblastic tumour (IMT) is an uncommon spindle-cell proliferation that occurs at various sites usually of children and young adults. We aim to highlight clinicopathological and epidemiological features of this uncommon tumour.
Method: We report a case of an IMT with an uncommon primary site.
Results: A ten-year-old boy with a history of immunodeficiency presented with a two-month history of discomfort in his right upper quadrant and right flank. A computed tomography scan of his upper abdomen revealed a 10 cm heterogenous adrenal mass compressing his liver. These appearances raised the possibility of a primary malignant tumour. A biopsy was performed showing a proliferation of spindled cells and histiocytoid cells arranged haphazardly and in fascicles with intervening thick collagen

bundles. There was an admixed moderate inflammatory cell infiltrate composed of lymphocytes, plasma cells and eosinophils. Mitoses were absent and no necrosis was seen. On immunohistochemical examination, the tumour cells were focally positive for smooth muscle actin and negative for anaplastic lymphoma kinase (ALK)-1 and CD1a.
Conclusion: IMT in the adrenal gland is rare with only few reports in the world's literature and must be considered in the differential diagnosis of radiologically suspicious adrenal masses.

PS-25-113
Metanephric stromal tumour: A report of a case with incidental diagnosis
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Objective: Metanephric Stromal Tumour (MST) is a rare renal neoplasm that mainly affects children. Our objective is to highlight the epidemiological, clinicopathological characteristics and outcome of this neoplasm.
Method: We report a case operated for renal artery aneurysm with an incidentally diagnosis of MST.
Results: A two-year-old boy had a prenatal diagnosis of malformative uropathy. The ultrasound and angiography showed a renal artery aneurysm. The patient underwent a left nephroureterectomy. The macroscopic examination showed a firm white renal tumour measuring 35 x 10 mm. Microscopically, the tumour was composed of spindle cells with a concentric arrangement around entrapped tubules and vessels. Some intratumoural arterioles showed angiodysplasia. On immunohistochemistry, the cells were positive for CD34 and negative for Desmin, Cytokeratin and PS 100.
Conclusion: MST is a rare benign tumour. Its characteristic microscopic appearance and immunohistochemical profile helps to differentiate it from other renal paediatric tumours. The originality of our case is due to the fact that the circumstance of discovery of the tumour is the renal artery aneurysm which is a consequence of angiodysplasia observed in this type of tumour.

PS-25-114
Clinicopathologic features of sporadic renal angiomyolipoma
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Objective: Renal angiomyolipoma (AML) is a triphasic benign mesenchymal tumour. It represents 1 % of removed renal tumours and is usually sporadic. Our aim is to present the clinicopathologic features of our series.
Method: We performed a retrospective study of 14 renal AML diagnosed at our department between 2008 and 2017.
Results: Our series included 13 female and one male patients. Mean age was 51 years old. AML was preoperatively suspected ($n = 9$) or incidentally discovered ($n = 5$). Tumour was solitary ($n = 11$) or multiple ($n = 2$). It was encapsulated in one case, non-encapsulated in 4 cases and ill-defined in 7 cases. The mean size was 4.2 cm (0.5–17 cm). AML was mainly lipoma-like ($n = 7$). Smooth-muscle cells were spindle ($n = 13$) or epithelioid-shaped ($n = 1$). Nuclear atypia was displayed in 6 cases and mitoses in one case. AML was associated with renal cell carcinoma ($n = 1$) and urothelial carcinoma of the ureter ($n = 1$).
Conclusion: Patients with sporadic AML tend to be older than those associated with tuberous sclerosis (50 versus 30–40 years old) and have larger lesions. AML seems to be hormonally induced since it occurs more frequently in women and expresses progesterone marker. Simultaneous AML and renal cell carcinoma is a rare occurrence.

PS-25-115
Rare upper urinary tract changes in a longstanding Bricker diversion
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Objective: Bowel segments and ureters for Bricker urinary diversions may display over time histological changes, of which the most common are related to intestinal mucosa. Ureteric changes are not well-documented. We report a case of intestinal metaplasia and dysplasia of the upper urinary tract and amyloidosis of the ileum.
Method: A 47-year-old male presented with bilateral pyonephrosis and ureteric dilatation. He had a Bricker urinary diversion performed at infancy for a neurogenic bladder induced by myelomeningocele. Imaging revealed non functioning kidneys. A bilateral nephrectomy at a two-month interval was performed.
Results: Grossly, kidneys were 7 and 9 cm in greatest diameter. Cut surface revealed destruction of the renal parenchyma and pyelocalyceal dilatation. Histological examination displayed features of chronic pyelonephritis. The epithelium of the upper urinary tract showed extensive colonic glandular metaplasia with foci of high-grade dysplasia immunoreactive for p53. The patient had a postoperative peritonitis and Bricker diversion as well as a part of the ileum were surgically removed. They displayed amyloidosis.
Conclusion: Intestinal metaplasia of the upper urinary tract is remarkably rare and has never been reported in Bricker diversions. It is considered as a premalignant lesion associated with adenocarcinoma. p53 expression signifies loss of cell cycle control and progression to dysplasia and cancer.

PS-25-116
Diagnostic utility of immunohistochemical staining for Ki-6, K5, K18, p63 and PSA in the differential diagnosis of malignant prostate
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Objective: Immunohistochemical methods are import part of oncological researches, as they supply specific visualization of localisation in tissues of various cells, hormones and their receptors, enzymes, immunoglobulins. They also allow to explore secretory and synthetic processes.
Method: The study of tissues of prostate was carried out (10 patients with prostate cancer, 10 patients with benign prostatic hyperplasia). Light microscopy and immunohistochemical analysis (PSA, p63, Ki-6, K5 and K18) of postoperative biopsies were performed.
Results: The activity in tissues at prostate cancer was revealed (p63). It was shown, that sprawls of round, oval and angular acinar structures, formed by one single-row light-colored epithelium with expression of PSA, were in stroma among glands. The expression in carcinomas at usage of K5 and K18 was revealed. In cases of usage of Ki-6, its slight activity was revealed.
Conclusion: This concept may serve as a valuable tool in the differential diagnosis of benign versus malignant glandular lesions of the human breast and salivary glands.

PS-25-117
Solitary fibrous tumour in urinary bladder : A rare case
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Objective: Solitary fibrous tumour (SFT) is a fibroblastic mesenchymal tumour. It develops from the serosal surfaces. Also, SFT may develop from sites which has no associate with the serosal surface. Solitary fibrous tumour is an uncommon neoplasia of the urinary bladder.

Method: We are presenting a case of 62 year-old female. She complained hematuria for a 2 month duration.Magnetic resonance imaging (MRI) showed 12x10 mm nodule that polypoid extension from the posterior wall of the bladder to lumen. Transurethral resection of the bladder was performed .
Results: The histopathology showed spindle-oval shaped cell proliferation in the collagenous stroma.On imunohistochemistry , these cells were positivite for CD34, BCL2, CD99 ,STAT 6 and negative for AE1/AE3, CD117 , CD31 and DOG1 .Ki-67 index was < 1 %. Immunohistochemistry features supported Solitary Fibrous Tumour.
Conclusion: Solitary fibrous tumour is very rare case in the urinary bladder. Histological and immunohistochemical examination are significant for diagnosis. The nuclear expression of STAT6 protein is highly sensitive for SFT. Thus, SFT can be differentiated from other spindle cell lesions.

PS-25-118
An interesting case of spermatocytic seminoma associated with maldescended testis
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Objective: Spermatocytic seminoma is a non-seminomatous tumour and usually it has no co-existance with crytorchidism.
Method: Forty-six year-old patient presented with testicular mass. He had an orchiopexy operation for crytorchidism 30 years ago.He has undergone orchiectomy.
Results: On the macroscopic examination of the orchiectomy specimen there was a well-demarcated 1.6x1.5x1.1 cm fleshy mass. Microscopic examination of the tumour revealed a polymorphic population of cells consisting of 3 types; giant cells, intermediate cells and lymphocyte-like tumour small cells. Tumour cells were all negative for CD 30, glypican 3,CD 117 and PLAP.
Conclusion: The diagnosis of spermatocytic seminoma is based on the typical morphologic features. But the pre-existing story of orchiopexy was a challenge for us because this tumour is not associated with crytorchidism. Nevertheless, our diagnose was ' spermatocytic seminoma.

PS-25-119
Tubulocystic chromophobe renal cell carcinoma (RCC): Expanding the differential diagnosis of renal neoplasia with a tubulocystic architecture
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Objective: Chromophobe renal cell carcinoma is often overlooked when it comes to the differential diagnosis of multiloculated cystic renal neoplasms. This unusual presentation helps put this entity into focus.
Method: A 49 year-old woman presented with left-sided flank pain and subsequent imaging showed a Bosniak IV cyst requiring a left radical nephrectomy. There were no other relevant past medical history events of note.
Results: We received a 400 gram left radical nephrectomy specimen which showed an upper pole well-circumscribed multiloculated cystic tumour. This measured 2.9 cm by 2.7 cm. Histopathological examination showed an oncocytic neoplasm with a tubulocytic architecture, showing only one focal solid island comprising a few irregular tubules. Examination under high power showed a few scattered perinuclear haloes and raisinoid nuclei. Immunohistochemistry showed diffuse and strong CK7 and CD117 expression with negative CD10, Vimentin , RCC and 34βE12 expression. This neoplasm was hence classified as a Grade II Tubulocystic chromophobe renal cell carcinoma.
Conclusion: Emerging reports show that the tubulocytic architectural pattern is shared by a variety of renal neoplasms, not exclusively pertaining to Tubulocystic renal cell carcinoma. These include oncocytomas, multilocular clear cell RCC and cystic nephroma. Chromophobe renal cell carcinoma is no exception and should be considered when confronted with this histological pattern.

PS-25-120
Tumour mimicking IgG4-related lesion in ureter
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Objective: IgG4-related disease (IgG4-RD), in spite of recent attention, has rarely been reported in ureter. It is characterized by elevated serum IgG4 and lymphoplasmacytic infiltrate with increased numbers of IgG4-positive plasma cells, regional fibrosis and obliterative phlebitis. We report a case occurred in ureter as tumour mimicking lesion. ureter as tumour mimicking lesion.
Method: 71-year-old male patient, suffering from hematuria, was done by right nephroureterectomy for the exploration of wall thickening lesion in ureter on CT scan. In the ureter, 2 cm-in-length wall thickening lesion was seen, and in the kidney, pelvis and calyces were dilated.
Results: Histologically, this ureter lesion showed diffuse lymphoplasmacytic infiltrates and fibrosis in myxoid background and focal obliterative phlebitis. These plasma cells showed IgG4 immunopositivity. Immunoglobulin (Ig) and Ig G4, evaluated postoperatively, were 1437 mg/dL and 99.3 mg/dL in each.
Conclusion: The recognition that IgG4-RD could cause tumour-mimicking lesion in ureter is clinically important as the pathologist should recommend to test patient's serum IgG4 level preoperatively and to screen the patient for signs of autoimmune disease.

PS-25-121
Mixed epithelial stromal tumour of the kidney. Report of a case
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Objective: Mixed Epithelial Stromal Tumour (ST) of the kidney is a recently recognized rare benign tumour with few cases reported either as MEST or under other terminologies such as cystic hamartoma of the renal pelvis and adult mesoblastic nephroma.
Method: A 49-year old woman was admitted with a history of chronic fatigue, anemia and a 3.3x2.9x2.9 cm solid, protruding mass on the lower pole of the left kidney discovered on MRI. The patient had a left partial nephrectomy. Gross examination of the specimen revealed a 38 mm well circumscribed, tan to yellow, partly solid and partly cystic mass.
Results: Microscopic examination revealed a biphasic tumour with intimate admixture of epithelial and stromal elements with areas having phylloides morphology. Spindle cells displayed alternating cellularity. The epithelial component consisted of epithelium lined cysts and clusters of small glandular structures. Both elements showed bland cytology. Stromal cells stained positively for SMA, Desmin, CD-10, Estrogen and Progesterone Receptors. Ki-67 stained less than 1 % of the cells. CD-34 as well as melanocytic markers staining were negative.
Conclusion: The diagnosis was MEST of the kidney. MEST is a tumour with distinct clinical and pathological features and is more common in perimenopausal women.

PS-25-122
Primary malignant melanoma of the bladder - a case report
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Objective: Malignant melanoma of the bladder as a primary tumour is rare, currently less than 30 cases were reported. More commonly they involve the urinary tract as metastasis, rather than as a primary tumour. We report a case of primary melanoma of the bladder.
Method: Patient was an 83 year-old women, presenting with hematuria, with no other relevant medical history. Abdominal ultrasound showed a solid mass in the distal ureter with nearby suspicious lymph nodes. Cystoscopy examination showed a lesion in the posterior wall. Transurethral resection of the bladder was performed.
Results: Histology revealed an ulcerative tumour composed of cells with severe nuclear pleomorphism, large eosinophilic nucleoli and scattered melanin pigment that invaded muscularis propria of the bladder wall. Mitosis were numerous and focal necrosis was present. Urothelial carcinoma "in situ" was absent. S100 protein, HMB-45 and Vimentin were expressed, whereas cytokeratins were not. The patient died 1 month later.
Conclusion: Upon morphology, imunohistochemical studies, and history of no previous biopsies or suspicious pigmented lesions, the diagnosis of primary malignant melanoma of the bladder was made. In this localisation, primary melanomas are rare and have a very poor prognosis.

PS-25-123
A confusing paratesticular neoplasm
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Objective: Paratesticular liposarcoma(PTLPS) is an extremely rare mesenchymal malignancy accounting for about 3–7 % of all paratesticular sarcomas. We herein report another case of PTLPS with a brief review of literature.
Method: A 60-year old man presented with a 3 months history of right scrotal mass. Testicular tumour markers were negative. Computerized tomography revealed a right-sided testicular 7,7 cm mass, a suspicious nodule of lung and a mesenteric lymphadenopathy. The patient underwent high orchidectomy.
Results: On gross examinationthe testicle measured 10x9x6cm, the epididymis 5 cm and the spermatic cord was distorted measuring 5,4 cm. A relatively circumscribed tumour of 8x8cm was identified in the paratesicular tissue. Cut surface was firm, white-yellow with polylobed borders. Microscopic examination revealed a mesenchymal malignant cell proliferation characterized by a dense fibrous tissue, with focally myxoîd changes. They contained dispersed spindle-shaped and stellate bizarre cells showing atypical and hyperchromatic nuclei. Fibrous septa also contained scattered mature adipocytes with hyperchromatic nuclei. A diagnosis of grade 1well-differentiated (sclerosing subtype) liposarcoma was made. The patient's post-operative course was uneventful. He had adjuvant radiation therapy. The patient remained recurrence and metastasis free at 24 months.
Conclusion: Preoperative diagnosis of PTLPS is difficult due to the confusion with benign adipose lesions. The most challenging issue is to make radical surgery to avoid recurrence.

PS-25-124
Sarcomatoid carcinoma of the urinary bladder: A rare variant of urothelial carcinoma: A report of two cases
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Objective: Sarcomatoid urothelial carcinoma (SUC) of the bladder is very rare as it accounts for 0.6 % of all bladder tumours. Our objective is to highlight the epidemiological, clinicopathological characteristics and outcome of this neoplasm.
Method: We report the cases of two patients diagnosed with SUC.
Results: Both patients were males. Patients' ages were 55 and 47 years. Tumours were large and infiltrative in both cases. Microscopic examination revealed tumours cells arranged in glandular pattern, alveolar pattern and nesting pattern. Many foci shows spindle shaped tumour cells having oval elongated nuclei. No areas of myxoid change were observed. areas of necrosis were noted in both cases. Immunohistochemical staining showed cytokeratin-positive epithelial component and vimentin-positive sarcomatous component.
Conclusion: SUC of urinary bladder is rare and aggressive neoplasm that has similar clinical presentation as that of conventional high grade urothelial carcinoma, but has worse prognosis. They present at younger age and at an advanced stage. Radical surgery along with chemoradiation improves the prognosis of the tumour.

PS-25-125
Carcinosarcoma of the prostate initially diagnosed as rectal sarcoma
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Objective: Carcinosarcoma of the prostate is a rare tumour and occasionally referred in bibliography. In our case a 80-years-old-man, presented with rectal bleeding. Endoscopy and CT scan showed a mass in the rectum.
Method: Microscopically, a spindle cell population was seen, with cytologic atypia and frequent mitosis. Immunochemically, the neoplastic cells were positive for actin and negative for cytokeratins, S-100 protein, HMB45, desmin, CD34, CD99 and CD117. The histological findings were compatible to a leiomyosarcoma, so a rectal leiomyosarcoma was presumed. At the same time, the patient complained of urination disorders so a prostatic biopsy was performed. The serum PSA was normal.
Results: Microscopically, a biphasic neoplastic population was found, consisted of spindle cells and epithelioid atypical cells. Immunochemically,the carcinomatous cells were positive for cytokeratins, PSA and PSAP and the spindle cells had the same immunoprofile as that referred above. The diagnosis of prostatic carcinosarcoma was established.
Conclusion: In conclusion, we present an extremely rare case of prostatic carcinosarcoma presented as a rectal soft tissue mass. One must always keep in mind the possibility of a prostatic primary when dealing with rare type of tumours which may protrude and invade rectum causing rectal bleeding. Applying proper immunohistochemical stains is crucial for the correct diagnosis.

PS-25-126
Correlation between CA19-9 immunohistochemical expression in transitional cell carcinoma of the urinary bladder and metastasis
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Objective: The prognosis of bladder tumours (BT) is still, in some cases, unpredictable despite the determination of grade and stage. Recent studies have highlighted the relevance of CA19-9 in determining the evolutiveness of BT. The aim of our work was to study the immunohistochemical expression of CA19-9 in BT and its correlation with tumour evolution peculiarly metastasis.
Method: We carried out a retrospective study of 56 cases of BT diagnosed following endoscopic resection and radical cystoporostatectomy between 2011 and 2013. Immunoexpression of CA19-9 in tumours was considered positive in the presence of intense or intermediate immunoreactivity with diffuse distribution. Correlation between CA19-9 immunoexpression and metastasis was assessed.

Results: Our results showed that the immunohistochemical expression of CA19-9 was not correlated with metastasis ($p = 0{,}19$).
Conclusion: In our series, the immunohistochemical expression of CA19-9 is not correlated with the occurrence of metastasis.

PS-25-129
SMARCB1 (INI1; BAF47) negative collecting duct carcinoma
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Objective: SMARCB1 protein represents a core subunit of the switch/sucrose nonfermenting chromatin remodeling complex which plays a critical role in transcription regulation. Loss of SMARCB1 protein is the consequence of biallelic inactivation of the SMARCB1 gene and it is observed in neoplasms that often exhibit rhabdoid features.
Method: A 53-year old male patient presented with haematouria and computed tomography revealed a 3.5 cm lesion in the right kidney. Right nephrectomy followed. No sickle cell trait was proven.
Results: The neoplasm was located in medulla with adjacent cortex infiltration and it was highly hemorrhagic. Histology revealed a cytologically high grade carcinoma with severe stromal desmoplastic reaction composed mainly by single-layered tubular structures with occasional hobnail cells, solid areas and a percentage of cells with rhabdoid features. Immunophenotypically the cells exhibited complete loss of the SMARCB1/INI1(BAF47) protein while they were positive for Pax-8, CK7, CK34βE12, SDHB, E-cadherin and pVHL. Vimentin, GATA3, CD10, TFE-3 and OCT3/4(POU5F1) immunostains were negative. The diagnosis of collecting duct carcinoma was established.
Conclusion: The differential diagnosis from renal medullary carcinoma was based upon the patient's age, the absence of sickle cell trait evidence and the appropriate histological features. SMARCB1/INI1 loss is observed in approximately 15 % of collecting duct carcinomas.

PS-25-130
A rare case of left inguinal hernia caused by a renal cell carcinoma (RCC) thrombus in the spermatic vein
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Objective: Unusual site metastasis as recurrence of renal cell carcinoma (RCC) has been reported in the literature. Metastatic tumour to the spermatic vein from RCC is unusual, with only occasional cases described in the literature. We present a rare case of RCC recurrence, presented as an inguinal hernia, due to histologically proven RCC thrombosis of the spermatic vein.
Method: A 76-year-old man was referred to our hospital due to a painful swelling of the left inguinal area, which was interpreted as hernial incarceration. Clinical examination revealed a firm-to-hard swelling of the left spermatic cord at the external inguinal ring A biopsy of the spermatic cord area was initially undertaken which was non diagnostic. Left orchiectomy was eventually performed.
Results: Histological examination revealed dilated and prominent blood vessels with thrombi of clear RCC due to metastatic tumour to the spermatic vein, with no testicular pathology. The patient had a history of left radical nephrectomy and tumour thrombectomy 2 years ago, due to RCC.
Conclusion: Inguinal/intrascrotal swelling is an uncommon symptom of RCC, due to tumour thrombus extending into the spermatic vein. A high degree of vigilence and a complete physical examination, including the spermatic cord is recommended during the follow up of RCC patients.

PS-25-131
Varicocele in children - to operate or not to operate: That is the question
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Objective: the question about necessity of children with early varicocele grade operative treatment still is not answered. Our study was devoted to revealing the varicous vein wall compensatory ability.
Method: we investigated vein intraoperative biopsies from 28 children with different varicocele grades. Light microscopy with picrofuchsin and Weigert's staining, immunohistochemistry were used.
Results: in early varicocele grade in middle and small vein walls we found predominantly external longitudinally SMC hypertrophy with diffuse wall thickening, one-sided multiple tall fibromuscular pillows. Well-formed elastic carcass—wall arterialization was present in large veins. Prominent intermuscular sclerosis with SMC band "coupling" was detected in middle vein walls in III varicocele grade. Fibrosis severity gave positive correlation with TGFβ1 overexpression and negative—with α-SMA expression.
Conclusion: compensatory vein wall remodeling was found in any diameter vein walls in early varicocele grade. We consider surgical approach to be reasonable in II and III varicocele grade, when progressive fibrosis and varicous vein wall rigidity induce heavy hemodynamic disorders, prolonged hypoxia and testicular atrophy.

PS-25-132
Idiopathic scrotal calcinosis - four patients
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Objective: Scrotal calcinosis (SC) is a rare and benign condition characterized by multiple asymptomatic and painless calcific deposits occurring in scrotum and formed as nodules and lumps within scrotal skin. The lesions have been attributed clinically as sebaceous cysts, fibroma, and xanthoma.
Method: Here is reported 4 patients with scrotal calcinosis at the institution. One of patients has observed relapsing lesion 6 years later.
Results: The patient's age range was 38–54 years. Two of them were solitary and two of them were multiple lesions. Measuring of the nodules was between 0,1 and 4 cm. One of the four patients had scrotal epidermoid cyst with intact epithelial walls. Varying stages of inflammation and foreign body giant cell reaction were seen around the scrotal calcinosis areas.
Conclusion: Although many mechanisms have been proposed in the pathogenesis, underlying mechanisms are still controversial at the present time. Some investigators suggest that SC is truly a late presentation of epidermal inclusion cysts that have undergone dystrophic calcification. So-called idiopathic scrotal calcinosis does not appear to be idiopathic, but rather a process of dystrophic calcification of epidermal cysts. But others reviewed the histologic data and found no evidence of an epithelial lining, residual cysts, and lipid or organisms, and concluded that the calcification was idiopathic introducing the term "idiopathic scrotal calcinosis."

PS-25-133
Leiomyoma of the prostate: A case report
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Objective: Leiomyoma is a rare tumour of the prostate that is diagnosed only by the histopathological and immunohistochemical examination. The differantial diagnoses of leiomyoma from other spindle cell lesions on prostate is difficult.
Method: We report a case of low grade smooth muscle tumour in a 66-year-old man who presented with obstructive urinary symptoms. The case was initially diagnosed as STUMP at a other center. Its H&E slides and parafine blocks was brought to our department for a consultation.
Results: Histopathological analyses showed the tumour composed of the proliferation of spindle cells, with moderately nuclear atypia and pleomorphism. Epithelial tissue was demonstrated at very limited area. Necrosis is absent. 0–1 mitosis was detected in 10 HPF. Immunohistochemistry demonstrated expression of SMA, desmin, caldesmon, MSA, pankeratin but no expression of CD34, CD117, bcl-2. Ki67 proliferation index was 15 %.
Conclusion: A leiomyoma of the prostate is a rare benign tumour of the prostate. Most cases are diagnosed at histopathological examination of prostate biopsies that have been done for benign prostatic hyperplasia. Differential diagnosis should consist of benign prostatic hyperplasia, STUMP, solitary fibrous tumour, stromal sarcoma, leiomyosarcoma and gastrointestinal stromal tumour.

PS-25-134
Prostatic melanosis: A case report
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Objective: Prostatic melanosis is a rare lesion that is characterized by melanocytic proliferation in prostatic stroma and the epithelium. This lesion is certainly benign and not a precursor of malignant melanoma but the pathogenesis of the lesion is uncertain. In this paper, a case of melanosis of the prostate and prostatic adenocarcinoma together in a 67-year-old man is described and differential diagnosis of the melanocytic lesions is discussed.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 67-year-old patient having 1 year history of prostatism symptoms. Laboratory test results were normal, except high Prostate Specific Antigen (PSA) level. Transrectal prostate needle biopsy reported that it was a prostate cancer with 3 + 4 = 7 Gleason score. After the evaluation, the patient went for a retropubic radical prostatectomy. Histopathological and immunhistochemical results were compatible with prostatic melanosis and prostatic adenocarcinoma.
Conclusion: Prostatic melanosis is a very rare lesion, only 20 reports of melanosis have been reported in the literature.Malignant melanoma should be kept in mind in differential diagnosis. However the clinical significance of prostatic melanosis is not clear, urologists and pathologists should be aware of its existence.

PS-25-135
Prognostic relevance of CA19-9 immunohistochemical expression in transitional cell carcinoma of the urinary bladder
I. Msakni*, F. Gargouri, M. Mhiri, A. Hajji, N. Mansouri, C. Kammoun, A. Bouziani, B. Laabidi
*Hôpital Militaire de Tunis, ANAPATH, Tunisia

Objective: The prognosis of bladder tumours (BT) is still, in some cases, unpredictable despite the determination of grade and stage. Recent studies have highlighted the relevance of CA19-9 in determining the evolutiveness of BT. The aim of our work was to study the immunohistochemical expression of CA19-9 in BT and its correlation with tumour grade, tumour stage and evolution (recurrence and metastasis.
Method: We carried out a retrospective study of 74 cases of BT diagnosed following endoscopic resection and radical cystoporostatectomy between 2011 and 2013. Immunoexpression of CA19-9 in tumours was considered positive in the presence of intense or intermediate immunoreactivity with diffuse distribution. Correlation between CA19-9 immunoexpression and tumour grade, tumour stage and evolution (recurrence and metastasis) was assessed.
Results: Our results showed that the immunohistochemical expression of CA19-9 was inversely proportional to grade and tumour stage. The majority of low-grade tumours (n = 27/32, 89 %) and the majority of superficial tumours (n = 35/50, 70 %) were positive for CA19-9. The correlation was statistically significant (p = 0,005 and 0,04 respectively). Recurrence and metastasis were studied in 56 patients. The immunohistochemical expression of CA19-9 was proportional to tumour recurrence. The majority of recurrent tumours (n = 16/18, 89 %) were positive for CA19-9. The correlation was statistically significant (p = 0,03). The immunoreactivity for CA19-9 showed no correlation with metastasis.
Conclusion: The CA19-9 seems to allow a better grading and could be useful for tumour staging. Moreover, this marker would be useful to better adjust the rhythm of the endoscopic control.

E-Posters

Sunday, 3 September 2017–Wednesday, 6 September 2017, 09:00–17:15, Hall 3

E-PS-01 Autopsy Pathology

E-PS-01-001
Post mortem examination of Dicephalus Parapagus Dibrachius Dipedis conjoined twins
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Objective: Conjoined twins are embryologic abnormalities which occur due to incomplete division of monozygotic twins. They are classified based on the most prominent site of union. Our objective was to use a post-mortem examination for classification and a detailed description of various co-existing pathologies present within the conjoined twins
Method: A 28-year-old gravida 3 Para 2 + 0 presented at the antenatal clinic of our hospital at a gestational age of 35 weeks. Her ultrasound report showed a conjoined twin pregnancy. There was a positive family history of twinning.
Results: An autopsy was performed following an early demise. The detailed morphological examination findings include a single atrium and single ventricle in Twin A, two ventricles in Twin B, dual pulmonary arteries and hypoplastic lungs in both twins and a single aorta arising from Twin B. Other anatomical findings are reported.
Conclusion: This report illustrates the occurrence of this variant of conjoined twins with a detailed description of an uncommon cardiovascular morphology/pathology not routinely encountered in these type of twins

E-PS-01-002
Incidental post-mortem finding of a vein of galen aneurysm following a road traffic accident mortality
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Objective: Vein of Galen aneurysmal malformations are rare childhood intracranial vascular anomalies. They account for less than 1 % of cerebral vascular malformations
Method: A 7-year-old male presented with post traumatic altered sensorium and quadriparesis. Head and neck examinations showed macrocephaly, occipital scalp abrasions. Glasgow Coma Score was 9/15. Both pupils were 3 mm bilaterally and reacted briskly to light. Cranial computed tomography (CT) scan was suggestive of obstructive hydrocephalus with a round spherical mass lesion in the pineal region. Clinical diagnosis of traumatic brain injury with incidental vascular malformation was made. He succumbed to his condition 12 hrs into admission.
Results: : At autopsy, the brain was enlarged with bilaterally symmetrical cerebral hemispheres. There was a fusiform aneurysmal dilatation of the left vein of Galen measuring 3.5 cm in length, causing a depression in the inferior surface of the temporal region of the left cerebral hemisphere. Both cerebellar tonsils were prominent. Coronal sections through the left cerebral hemisphere showed expansion of white matter with a markedly dilated lateral ventricle. Focal areas of contusional hemorrhages within grey and white mater of the cerebral hemispheres were seen.
Conclusion: We report a case of an incidental finding of a rare vein of Galen aneurysm.

E-PS-01-003
The dark side of the brain - an autopsy case
P. Sequeira*, A. Souto, H. Coelho, J. Oliveira, J. Nogueira, A. Oliveira
*Hospital Garcia de Orta, Anatomia Patológica, Almada, Portugal

Objective: Case of leptomeningeal melanomatosis, involving the brain and cranial nerves of a patient presenting with anorexia and vomiting.
Method: A 53-year-old asian male presented to our emergency department with a 1 month history of anorexia and incoercible vomiting. A head CT scan was performed, which revealed multiple solid pontine lesions in relation with the fifth cranial nerve, later confirmed by MRI. A bone marrow aspiration and lumbar puncture were performed, both unremarkable. Within a few days the patient abruptly died, which prompted an autopsy request.
Results: Upon autopsy, the leptomeninges of the fronto-temporo-parietal cortex, brain stem and cranial nerves were diffusely thickened by a black lesion. No mucocutaneous pigmented lesions were found. Histology showed a diffuse proliferation of epithelioid cells, with marked anisokaryosis, prominent nucleoli and a heavy cytoplasmic melanocytic pigment in the leptomeningeal space, with focal invasion of the underlying cortex. Immunohistochemically, the cells showed a positive expression for pS100, HMB45 and MelanA.
Conclusion: Leptomeningeal melanomatosis is a rare primary melanocytic CNS neoplasm arising from the leptomeningeal melanocytes, associated with a poor prognosis. It should be distinguished from metastatic malignant melanoma and other central nervous system tumours that undergo melanization such as schwannoma, medulloblastoma, or paraganglioma.

E-PS-01-004
Complex cyanogenic congenital heart disease associated with 21 trisomy - case report
S.-A. Ghitoi*, M. Aschie, I. Poinareanu, G.-C. Cozaru, A. F. Mitroi, M. Enciu, G.-I. Baltatescu, O. Cojocaru, A. A. Nicolau, A. Chisoi, D. Aschie
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Objective: Congenital heart diseases are those abnormalities of the heart and/or the great vessels that are present at birth. They show up with a relatively high incidence, accounting for at third of all congenital diseases and affecting on average 7–8 children of every 1000 liveborn infants. Lesions range from relatively asymptomatic to rapidly fatal.
Method: The paper displays the case report of a female premature infant born in Constanta Clinical County Hospital, autopsied in the Pathology Department.
Results: The clinic case we present here is a premature infant with Down syndrome, initially suspected based on the facial dimorphism, who was confirmed by karyotyping techniques. This baby showed multiple congenital heart diseases such as atrial-ventricular duct, complete type, Fallot tetralogy and severe pulmonary hypoplasia. The clinic and genetic examination of the patient was later confirmed following autopsy.
Conclusion: The most common abnormalities of all are ventricular septal defects, atrial septal defects and patent ductus arteriosus which also is the most frequent congenital heart disease of the premature infants. Everyone of these abnormalities can occur as only event or as a component of various genetic syndromes.

E-PS-01-005
Histological characteristics of incidental meningiomas in forensic autopsy
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Objective: Meningioma is the most common intracranial tumour which arises from the arachnoidal cells or meningothelial cells. Our study aimed to characterize the histopathological features and WHO grading distribution of incidental meningiomas, in a forensic autopsy study.
Method: The reports from autopsies performed in the last 4 years, in our Department, have been reviewed, selecting 17 tumours exhibiting gross features of meningiomas. Routine and special stains (Trichrome, PAS, and Alcian blue) have been performed.
Results: The diagnosis of meningioma has been confirmed in 16 cases, representing approximate 0.4 % in our files. The age distribution ranged between 53 to 90 years old, with a male predominance (81.25 % vs. 18.75 %). Fifteen undiagnosed intracranial tumours have been diagnosed as meningiomas grade I (meningothelial, transitional, and psammomatous types) and one tumour as grade II (clear cell type). Although gross features suggested a meningioma, one of the tumours revealed microscopical features of metastatic malignant melanoma consistent with the medical history.
Conclusion: Incidental meningiomas are relatively rare in forensic pathology. Their diagnosis is of great relevance, since their histopathological features may favor brain hemorrhage and may be related to the cause of death. Microscopical diagnosis may differentiate them from other types of tumours, in correlation with the clinical information.

E-PS-01-007
Hamartoma of mature cardiac myocytes (HMCM): An autopsy case report
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Objective: HMCM is a rare benign lesion of the myocardium characterised by localised, disorganised and hypertrophied mature cardiac myocytes. Case report: 39 years old healthy woman was admitted to department of neurosurgery for intracranial bleeding caused by rupture of aneurysm of a. communicans anterior. She died 8 days after admission due to edema of the brain and bronchopneumonia. ECG showed only nonspecific changes suggestive of mild anteroseptal left ventricular hypertrophy. An incidental autopsy finding was a whitish unencapsulated tumour in the anterior wall of the left ventricle and adjacent part of ventricular septum protruding above the plane of section.
Method: Histological slides were stained with H&E, blue trichrome and antibodies against CD 31 and Factor VIII.

Results: Histologically the tumour consisted of various different forms of disorganized mature hypertrophic cardiac myocytes without vacuolization, somewhere creating "herringbone" pattern. Dilated venules, thickened coronary arteries and intervening bands of connective tissue were present among cardiomyocytes. The findings were compatible with diagnosis of HMCM.
Conclusion: Clinical manifestations of HMCM include disturbances of cardiac rhythm, intracavitary cardiac obstruction or alteration of myocardial contractility, and some cases may be clinically silent, therefore the incidental findings at other patient examination or at autopsy.

E-PS-01-008
Sudden death from A/H1N1 in Northern Greece: Autopsy and histopathological findings
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Objective: Novel influenza A (H1N1), which is also called human influenza virus with swine origin, has created a major worldwide health problem and has high mortality and morbidity around the world.
Method: We present an autopsy case of a sudden, out-of-hospital death, of a middle-aged male, fireman in profession, with no underlying disease. Fever was his only symptom. He was prescribed antibiotic therapy and collapsed at home, 5 days later, with dyspnea. Prior to the autopsy his unit doctor informed us that another fireman with fever was transferred to hospital.
Results: The autopsy was performed following conventional protocol with the initial precautions. Tissue samples from all major organs were collected and fixed in formalin. Nasopharyngeal swabs were taken, sent to the National Influenza Reference Center and found positive for A (H1N1).
Conclusion: The main cause of death from influenza A (H1N1 infection) is acute respiratory distress syndrome. Sudden influenza death cases involve mostly young, apparent healthy persons so can be misdiagnosed, raising medico-legal problems.

E-PS-01-009
Pheochromocytoma and myocarditis revealed at autopsy after sudden death: What was the cause of death?
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Objective: To report a puzzling case of pheochromocytoma associated with myocarditis and suppurative pneumonia discovered after a sudden death and to discuss the putative mechanisms of death.
Method: The autopsy and pathological findings in a young male with sudden death are described with a review of the related literature.
Results: A 33 year-old-man, who had a smoking habit of 20 cigarettes per day. His medical history was unremarkable except for an allergy to penicillin. He had been complaining, about cough, dyspnea, hemoptysis and fever since 1 week. He was admitted to the Emergency Department for exploration. A few hours later he presented a cardiac arrest and was declared deceased. The autopsy revealed hemorrhagic pulmonary edema, heterogeneous aspect of the myocardium and a left adrenal mass measured 10 cm of large. The histologic examination confirmed the presence of a diffuse alveolar edema with foci of suppurative alveolitis, focal lymphocytic myocarditis and an adrenal pheochromocytoma.
Conclusion: Sudden death resulting from adrenergic myocarditis induced by pheochromocytoma is a rare but well known condition. However the differential diagnosis with an infectious myocarditis can be challenging as in our case.

E-PS-01-010
Sudden death due to a primary mediastinal large B-cell lymphoma
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Objective: Sudden unexpected death due to clinically undiagnosed neoplasia in young adults is a rare phenomenon. We report a new case of sudden death resulting from a mediastinal B-cell lymphoma.
Method: The autopsy and the histological findings in a young male with sudden death due to a previously unrecognized primary mediastinal large B-cell lymphoma are described with a review of the related literature.
Results: A 25-year-old man with history of shortness of breath in the last 3–4 months. On the day of his death he presented a severe dyspnea and a loss of consciousness. He was declared dead at the emergency despite the reanimation. The autopsy revealed a cyanosis of the face, cerebral edema, anterior mediastinal mass infiltrating the pericardium and extending to the thoracic cage and the sub-hyoid region. The histological findings of autopsy specimens revealed the presence of mediastinal large B-cell lymphoma and a hemorrhagic alveolar edema.
Conclusion: Mediastinal large B-cell lymphoma is a rare cause of sudden death in young adults. Our case demonstrates that a patient may have minimal symptoms in the presence of significant disease. It also highlights the need for a thorough autopsy examination in cases of a sudden unexpected death in young adults and children.

E-PS-01-011
Sigmoid colon adenocarcinoma involving left testis within an inguinal hernia causing peritonitis and septic shock
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Objective: Direct involvement of the testis by rectosigmoid adenocarcinoma is very rare. This case also illustrates the event of peritonitis originating within an inguinal hernia, due to a pT4 carcinoma, which often escapes clinical detection.
Method: An 80 year-old man was described by his wife as having suffered a 2-day history of abdominal pain, nausea, vomiting and loose stools, as well as foul-smelling urine. She also noted abdominal distention and increasing shortness of breath, after which he collapsed at home. Initial resuscitation was successful but the patient remained in haemodynamic shock and passed away a few hours later. The patient was a known COAD and heart failure case.
Results: Post-mortem examination showed paralytic ileus, a few bowel loop adhesions and a large left inguinal hernia. Exploration of the latter showed that most of the sigmoid colon was located within the inguinal hernia sac, and showed a mass with extensive overlying fibrinous serosal exudate. The left testis was embedded on the serosal surface of this mass. Sectioning showed a tumour of the colon reaching the serosal surface and testicular hilum. Histological examination showed an intestinal type adenocarcinoma, pT4, which also directly spread into the testicular hilum and epididymis, but not into testicular parenchyma.
Conclusion: Colonic carcinoma can involve the testis by retrograde venous extension or embolism, retrograde lymphatic extension, arterial embolisation and direct tumour invasion. This unusual case highlights the potential risks of inguinal hernias harbouring malignancy that escapes early clinical detection.

E-PS-01-012

Sudden death due to a cerebellopontine angle epidermoid cyst

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Objective: Epidermoid cysts (EC) of the brain are uncommon tumour-like lesions, most often of congenital origin. We Report a rare case of sudden death due to large intracranial cerebellopontine angle EC.

Method: The autopsy and histological findings in an adult male with sudden unexpected death resulting from an EC of the brain are described with a review of the related literature.

Results: A smoker 58-year-old man, presented a month before his death, with behavioral disorders with notion of repeated fugue. He was found dead in the public street. The external examination of the body revealed the presence of a bilateral convergent strabismus and absence of traumatic lesions. The autopsy showed cerebral edema and a cystic mass of the cerebellopontine angle compressing the brainstem. Histologic examination of this mass concluded to an EC. Death would therefore be the consequence of tonsillar herniation due to a rapid increase of the intracranial pressure.

Conclusion: Intracranial EC are uncommon brain tumours that account for 0.2 to 1.8 % of all intracranial tumours. Approximately half of these cysts are located at the cerebellopontine angle. They are usually symptomatic and therefore easy to diagnose. However, in rare cases they can lead to death if they are unrecognized.

E-PS-01-013

Metastatic lung cancer: A misleading presentation

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Objective: We present 49 y/o women without history of interest that came to our emergency room with a pontine haemorrhage. During admission procedure patient's condition kept declining. Imaging tests revealed multiple brain lesions, reported as cavernomas and a mass in the right lung. A fine needle puncture aspiration of the lung lesion was performed and diagnosed of non-small-cell lung carcinoma. After 5 days in hospital the patient died

Method: The post-mortem examination revealed a 5,5 cm diameter tumour in the right lung hilium, composed of large cells in a glandular arrangement with lymphovascular invasion. The immunohistochemistry study was positive for CK7, Ber-Ep4 and MOC 31. According to histology and immunophenotype a diagnosis of lung adenocarcinoma was established. Brain lesions showed clusters of neoplasic cells intermingled with fibrin, representing tumour emboli.

Results: The fundamental process was a lung adenocarcinoma which produced multiple hemorrhagic metastases in the brain, brainstem and cerebellum. The immediate cause of death was a hemorrhagic pontine metastasis. Moreover, we demonstrated bilateral bronchopneumonia, hemorrhagic infarctions and lung edema.

Conclusion: This is an example of a misleading presentation of a lung cancer, which lead to the misdiagnosis of the patient and a fatal outcome.

E-PS-02 Breast Pathology

E-PS-02-002

Androgen receptor expression in triple-negative breast cancer

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Objective: Triple-negative breast cancer (TNBC) has a poor prognosis because of frequent recurrence. Androgen receptor (AR) is involved in the pathogenesis of breast cancer, but its role is not clearly defined. In spite of this, the interest of researchers in using the androgen receptor as a prognostic and potential therapeutic target in TNBC is constantly growing.

Method: 43 cases of triple-negative breast cancer were randomly selected to determine the presence of androgen receptors using an immunohistochemical method. The age of the patients was 32 to 61 years, the study was performed on tumours of patients who had not previously received chemotherapy, hormone therapy or radiotherapy.

Results: 8 patients (18,6 %) of the 43 studied cases was revealed prominent expression of androgen receptors in tumour cells. A decision was made to prescribe an additional line of antitumour therapy TNBC - antiandrogen therapy.

Conclusion: AR expression may be useful as a marker for inclusion in treatment androgen synthesis inhibitor or synthetic non-steroidal antiandrogen in TNBC patients. The subsequent study of the role of AR and its relationship with clinicopathologic features in TNBC will be conducted.

E-PS-02-003

Malignant melanoma in the breast: A case report

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Objective: Malignant melanoma mostly occurs in the skin, mucous membranes and choroid. Melanoma in the breast is a rarely seen entity.

Method: An 84-year-old female presented to our General Surgery department with a complaint of lump in her left breast and axilla. Ultrasound revealed a dense, cystic lesion (BIRADS IV) in the retroareolar area and a radiopathological lymph node in the left axilla. She underwent modified radical mastectomy.

Results: The gross examination revealed a 6.5 cm tumour located under the areola expanding into the lower quadrant. Microscopically, the tumour cells were round/oval with large nuclei and nucleoli and abundant cytoplasm. Immunohistochemical profile of the tumour was compatible with malignant melanoma. There was no tumoural invasion on the breast skin. Invasion was detected in 2 of the 11 resected lymph nodes. No cutaneous or mucosal lesions of malignant melanoma were detected clinically and radiologically after the surgery.

Conclusion: Malignant melanoma in the breast may simulate other malignancies; the case we report here raises the awareness of malignant melanoma and points out that it should always be kept in mind in rare locations as well as the breast.

E-PS-02-004

Bilateral metachronous breast malignancies: Phyllodes tumour and NST carcinoma. Case report and literature review

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Objective: To describe the clinicopathologic features in a case of a Phyllodes tumour, a rare type of stromal tumour of the breast and a metachronous breast carcinoma.

Method: We present the case of a 68 years old patient with a palpable nodule in her left breast. After clinic and imagistic investigations that shown a BIRADS score of 3–4, a sectorectomy was performed. Histopathologic examination reveald a Phyllodes tumour, borderline. The breast tissue from the periphery of the tumour presented some areas of florid intraductal hyperplasia and an intraductal papiloma. Two years later, the patient came back because of another nodule in her right breast,

evaluated as BIRADS 5 and a mastectomy was performed. At section a 3 cm white, firm nodule with infiltrative borders was found . HP exam revealed a breast carcinoma, NST, grade II, N2a. The IHC reveals a ER 20 % and no PR expresion while Cerb 3+ was diagnostic for HER2neu positivity.
Results: Phyllodes tumour is not a risc factor for breast carcinoma ,but if high risk lesions for malignancy coexist, a periodic bilateral follow up should be made.
Conclusion: Our case report aims to provide a better understanding of carcinogenesis when both components, epithelial and stromal, develop metachronous malignancies.

E-PS-02-005
Is oral cavity a preferred place of breast metastasis? Report of 2 cases and literature review
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Objective: We present the case of two pacients from ENT department with brest metastases in the alveolar crest, respectively, salivary gland.
Method: First patient, aged 76, with a previous mastectomy 23 years ago for breast carcinoma, presented an enlarged salivary gland. The second patient aged 61, with history of breast carcinoma 4 years ago, presented an ulcerated gingival tumour. The histopathologic examination confirmed in both cases metastasis from breast carcinoma.
Results: In the first case, a proliferative process with trabecular pattern was found. GCDFP-15 and WT-1 was negative. Knowing the medical history of the patient, ER was also tested and found 90 % positive. The PR was repeatedley negative. In the second case, the salivary gland was infiltrated by a proliferative process with a tubuloglandular pattern. The IHC tests confirmed the suspicion of metastic breast carcinoma, with ER positive 90 %, PR positive 65 % and Cerb negative. Other differential diagnosis from a primary ENT area malignancy were excluded.
Conclusion: : In the ENT area the breast metastases are extremly rare and can be mistaken with a primary salivary gland ductal carcinoma. Our cases are also relevant for the differences in progression, considering that in the first patient metastasis appeard after 23 years while in the second case after only 4.

E-PS-02-006
Case report of a primary well differentiated neuroendocrine tumour (carcinoid tumour) in the breast
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Objective: Diagnose a 4 cm mass, found in the right breast of a 73 year old lady, using routine and immunostains.
Method: The specimen was fixed in a formalin solution, neutral buffered 10 %, sufficient sections were obtained from the mass that showed a cut surface of whitish-gray solid tissue. H&E stained sections were prepared, . Immunohistochemistry was appllied.
Results: The microscopic study revealed a proliferation of small nests and trabeculae of monotonous cells having round-ovoid nuclei with eosinophilic granular cytoplasm and granular chromatin, no necrosis could be seen. IHC revealed positive reaction for Chromogranin, Synaptophysin, negative result for CK-HMW, CK5-6, CK7, E-Cadherin, c-kit, and CD99; Ki-67 showed low index (about 2 %).
Conclusion: The tumour was diagnosed a well differentiated neuroendocrine tumour (carcinoid tumour), primary in the breast, no other lesions could be detected in other sites confirmed by negative CT and PET-scan.

E-PS-02-007
Primary occult breast carcinoma: A clinicopathological challenge
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Objective: To present the case of a rare pathology and the clinicopathological challenges that arise, as well as the dilemma that the consensus in the therapeutic decision represents
Method: A 75-year-old woman, with no relevant pathological history. In September 2016 consulted for a nodule with 4 mm in the left upper outer quadrant. Mammography and mammary ultrasound Bi-rads 2. A biopsy was performed and the anatomopathological report was a lesion of uncertain potential of malignancy. In a multidisciplinary meeting it was decided to perform a lumpectomy, which at the histological examination revealed a lymph node with metastasis due to an adenocarcinoma with morphological and immunohistochemical characteristics compatible with mammary origin.
Results: With this diagnosis, MRI was performed without tumour evidence, and also new breast biopsies were performed, negative for neoplasia. On the other hand, studios were also made to rule out other possible neoplastic foci (genitourinary, digestive, pulmonary), all of which were negative. In a new multidisciplinary meeting, a mastectomy was then decided, which revealed no tumour at the histopathological examination.
Conclusion: Primary occult breast carcinoma, being less than 1 % of breast carcinomas, is a very difficult diagnosis and lacks of guidelines. For this reason it requires a great intellectual and technical effort, as well as a coordinated and effective multidisciplinary work that leads to the decision that can offer greater benefit to the patient.

E-PS-02-008
Post-neoadjuvant chemotherapy (PNACT) breast histiocytosis mimicking metastatic carcinoma
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Objective: To describe specific morphological changes in the breast related with PNACT.
Method: 63-year-old female diagnosed with invasive ductal carcinoma underwent 4 courses NAC followed by a quadrantectomy with sentinel lymph nodes dissection. All specimens were evaluated by routine hematoxylin-eosin sections and additional immunohistochemical (IHC) stainings.
Results: On the needle biopsy a tripple negative invasive ductal carcinoma G3 was found. The breast specimen received after NACT demonstrated areas of fibrosis with proliferation of small cells with pale cytoplasm and hyperchromatic nuclei. The same cell proliferation was identified in the three lymph nodes. IHC stains showed a negative reaction for PR, ER, HER-2, S-100, CK AE1/AE3 and E-Cadherin in the suspected cells and only CD 68 was positive The diagnosis of the PNAC breast histiosytosis was set.
Conclusion: The PNACT parenchymal histiocytosis may mimick primary and metastatic malignant diseases as a clear cell kidney carcinoma, histiocytoid (myoblastomatoid) variant of lobular carcinoma and lipid rich breast carcinoma. The comprechensive medical information, careful histological analysis with the support of IHC play an essential role in the correct morphological diagnosis.

E-PS-02-009
Change of Her2/neu protein expression level and Her2/neu status in local metastases of breast cancer with its equivocal (2+) expression in primary tumour
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Objective: To compare Her2/neu protein expression and Her2/neu statuses of primary breast cancer (BC) and its local metastases in cases with equivocal (2+) expression of this marker in primary tumour (PT).
Method: Her2/neu immunohistochemical study (Ventana) of PT and local metastases by 25 BC patients with equivocal (2+) Her2/neu expression in PT was performed. Her2/neu gene amplification in PT was evaluated by SISH (Ventana). ASCO/CAP guidelines were used. Her2/neu expression and statuses of PT and metastases were compared using Wilcoxon and McNemar tests.
Results: Of 25 studied cases in 80 % Her2/neu expression in metastases was lower (0, 1+), in 4 % higher (3+), in 16 % the same (2+) if compared with PT. Her2/neu expression median was 1+ (IQR 1) in metastases, difference with PT was significant ($p < 0.001$, Wilcoxon signed rank test). Of 25 studied cases 20 % had amplified Her2/neu gene in PT and in 4 % metastasis had 3+ protein expression. No significant difference was found when Her2/neu statuses of primary and metastatic tumours were compared ($p = 0.125$, McNemar test).
Conclusion: In BC with equivocal (2+) Her2/neu expression in primary tumour significant decrease of its expression in metastases was discovered, while Her2/neu statuses of primary and metastatic tumours were the same (negative) in the majority of cases.

E-PS-02-010
Refining the accuracy of primary and metastatic breast cancer diagnosis: An immunohistochemical assessment of myoeptithelial cells following tissue microarray (TMA) application
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Objective: The aim of our study was to evaluate myoepithelial cell immunophenotype in breast cancer and to conduct a comparative assessment between TMA technique and classical methods of specimen processing.
Method: 66 blocks containing primary tumours and corresponding metastases were used in our study. 5 cores of tumour tissue were extracted from each block and implanted in recipient blocks using TMA technique resulting in a total number of 13 blocks. Slides were processed for routine histopathological diagnosis. ER, PR, HER2, CK5 were assessed for the molecular diagnosis followed by p63, SMA, S100, Ki67, p63/SMA and S100/Ki67 evaluation.
Results: Histopathological diagnosis revealed ductal and lobular invasive carcinomas that were classified as luminal A, followed by luminal B, triple negative (CK-) and HER2+. p63 had an isolated expression whereas SMA was expressed in the majority of cases. p63/SMA co-expression was restricted to a few specimens. S100 was mostly negative while Ki67 expression prevailed. S100/Ki67 co-expression was also restricted.
Conclusion: We hereby support the benefits of TMA large scale usage in order to ensure the refinement of breast cancer diagnostic approach through selection of hot-spot tumour areas.

E-PS-02-011
Morphological and immunohistochemical features of breast cancer in postmenopausal women
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Objective: Breast cancer is a concearning health issue with high mortality rate worldwide. Our purpose is to establish the morpho-clinical and immunohistochemical profiles of malignant breast tumours in postmenopausal women.
Method: A retrospective study was performed in order to identify female patients older than 55 years diagnosed with breast cancer over a period of 3 years. We analyzed the clinico-pathological and immunohistochemical characteristics of these tumours.
Results: We have gathered a number of 99 cases: 97 primary carcinomas (74 of wich were IDC-NOS) and 2 secondary tumours. 46 % of the total were larger than 2 cm and 14 % were poorly differentiated (G3). Axillary dissection was performed in 35 % and nodal metastasis was identified in 27 % of cases. Lymphovascular invasion was present in 32 %, while perineural invasion was identified in 18 % of cases. 54 % of the tumours were of luminal B subtype (23 % in the 55–64 age group, 16 % in the 65–74 age group and 15 % over 75 years), 22 % of luminal A, 17 % triple negative and 7 % with HER 2 positivity.
Conclusion: Breast cancer in postmenopausal women seems an aggressive malignancy, being associated with adverse pathological factors and requiring adapted therapeutical strategies.

E-PS-02-012
Morphotypes of the triple-negative breast cancer
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Objective: Triple-negative breast carcinomas (TNBCs) are a very morphologically heterogeneous group of breast carcinomas with none or minimal expression of estrogen and progesterone receptors and no HER2 protein over-expression or HER2 gene amplification. The aim of this study was to evaluate the correlation of TNBC morphotypes with selected clinico-pathological parameters.
Method: In this study, we re-examined the morphological features of TNBCs obtained from mastectomies diagnosed in our department from 2010 to 2016. We analysed the association of morphology to age, lymph node involvement, distant metastases, relapse free and overall survival.
Results: In this sample the majority were invasive breast carcinomas with medullary features circumscribed by a massive fibrotic core, a large central necrosis/fibrosis and numerous tumour infiltrating lymphocytes (72 %). In various parts of the tumours, the tendency to spindle cell and/or apocrine differentiation (transformation) was frequently observed. Only a minority of tumours showed the morphology of secretory carcinoma or invasive micropapillary carcinoma (16 %), though areas with extensive fibrosis and lymphocyte infiltration were seen. Td the morphology of metaplastic carcinoma with chondroid, osseous or other type of mesenchymal differentiation observed in some reports missing. There was no significant association between tumour morphology and clinico-pathological parameters.
Conclusion: In general, in all examined TNBCs we could see extensive fibrosis, occasionally with necrosis which could be a result of intensified immune reaction accompanied by lymphocyte infiltration. In spite of prevailing high proliferative activity measured by Ki-67, a minority of patients had lymph node or distant metastasis at the time of diagnosis.

E-PS-02-013
Interobserver agreement in the classification of ductal carcinoma in situ of the breast: Study design
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Objective: The incidence of ductal carcinoma in situ of the breast (DCIS) has greatly increased due to population-based breast cancer screening. DCIS is almost always treated to avoid invasive breast cancer development, yet it is highly likely that many DCIS lesions do not show progression if left untreated. Risk stratification is necessary to avoid overtreatment and therefore this study explores the value of pathologic findings by evaluating interobserver agreement.
Method: A random sample of 360 patients from a population-based, nationwide cohort of 2,767 women diagnosed with screen detected pure DCIS

between 1993 and 2004 and conservatively treated (with or without radiotherapy) were included. All women who developed ipsilateral invasive breast cancer were also included (n = 202; approximate median follow-up 10.7 years). Tissue blocks are collected from the DCIS lesions. The following pathologic variables will be digitally scored by European (breast) pathologists: grade, mitotic rate, calcification, necrosis, stromal and inflammatory response. Interobserver agreement will be analysed.
Results: Tissue blocks from 85 % of the involved Dutch hospitals could be collected and from these 40 % has been revised. Twenty pathologists have agreed to participate.
Conclusion: Interobserver agreement in the classification of DCIS will determine whether pathologic variables can be safely used for reliable risk stratification.

E-PS-02-014
Workload impact of automated image analysis and deep learning on manual screening of sentinel node biopsies in breast cancer
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Objective: Our aim of this study is to evaluate whether digital image analysis (DIA) and deep learning (DL) can decrease the workload for the examining pathologist when screening sentinel node biopsies (SLNB) in breast cancer (BC) - without compromising the diagnostic accuracy.
Method: From a cohort of 135 patients with BC receiving surgery, SLNB were collected from Dept. of Pathology Rigshospitalet, Odense and Slagelse, Denmark according to national and international guidelines. Tissue samples were submitted for frozen section procedure, where serial sections were stained locally with immunohistochemistry (IHC) and hematoxylin and eosin (H&E). Stained sections were digitized and analyzed using a DIA algorithm for IHC cytokeratin (CK) and a DL-based algorithm for H&E.
Results: Conventional microscopy was used as golden standard and compared with DIA and DL. The IHC-CK algorithm demonstrated a sensitivity of 100 % (i.e. no false negative slides were observed). On average, the workload could have been decreased by 58.2 % by using DIA as a screening tool. We aim to include results from H&E DL algorithm in the future.
Conclusion: Our proposed IHC-CK algorithm is an ideal screening tool for SLNB, and implementation of DIA has already shown a decrease in workload for examining pathologists by over 50 %.

E-PS-02-015
Cell density in phyllodes tumours
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Objective: Phyllodes tumour and fibroadenomas are group of neoplasm consisting of proliferation of both epithelial and stromal component. Fibroadenomas are considered as totally benign lesion, as to phyllodes tumours can be devide into benign, borderline and malignant categories based on histological appearance. One of the criteria used to determine all three category is the degree of stromal cellularity.
Method: The study included 57 phyllodes tumour treated 2008–2016 in Petrov oncology institute. We analyzed a total number of stromal neoplastic cells in phyllodes tumour from a 1 sq mm sample of histology slide using scanned images and image analysis software.
Results: Mean absolute neoplastic stromal cells in 1 mm2 of histology slide was in benign lesions 2944.67 ± 337.74 / mm2, in borderline samples 3493.00 ± 1000.42/ mm2, in malignant phyllodes tumours 4141.96 ± 397.06/mm2. As a control we used usual fibroadenomas and cell density in usual fibroadenomas was 2148.71 ± 577.35/mm2, a bit lower than in benign phyllodes tumours.
Conclusion: Image analysis of cell dencity is a good and objective tool to determinate cell density in phyllodes tumours.

E-PS-02-016
Assessment of biomarker changes in breast cancer in initial, intermediate CNB and in resection specimen after neoadjuvant chemotherapy
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Objective: We performed analysis of histology changes within tumour before, during and after neoadjuvant therapy.
Method: The study included 51 breast carcinomas before, during and after neoadjuvant therapy. We have analyzed hormonal receptors, Ki67 and HER2 status changes before, during (after 2 cycles NCT) and in resection specimen. We did not perform any IHC stain in cases with pCR.
Results: The Ki67 level in initial biopsy was 46,86 %, in intermediate CNB after 2 cycles of neoadjuvant therapy Ki67 was decreased to 22, 64 % (p = 0,000791) and in resection specimen Ki67 index in residual cancer was 27,8 % with no significant differs between intermediate and resection specimens. As to ER status there was no significant changes in three different settings in tumour race. ER " + " was 63 %, 67 %, 66 %; PR " + " 54 %, 50 % 66 %; and HER2 negative 83 %, 79 % 85 % respectively.
Conclusion: During neoadjuvant chemotherapy there was the most significant changes in KI67 index, other biology markers did not change neither during or after neoadjuvant therapy.

E-PS-02-019
PD-1, PD-L1 and CTLA-4 in pregnancy-related - and in early-onset breast cancer: A matched case-control study
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Objective: Immune-checkpoint markers (ICM) are promising potential therapeutic targets in early-onset (young women with breast cancer-YWBC) and pregnancy-related breast cancer (PRBC). Our aim was to compare immunohistochemical expression of PD-1, PD-L1 and CTLA-4 of PRBC and YWBC, and their prognosis prediction potential was correlated to that of conventional clinicopathological factors.
Method: Twenty-one PRBC cases were paired with 21 YWBC. ICM were evaluated by immunohistochemistry (IHC) on whole slides. IHC score was defined as the percentage of positive cells, assessed separately among tumour cells, intratumoural lymphocytes and peritumoural lymphocytes.
Results: Neither of the investigated ICMs showed significant association with any of the conventional clinicopathological factors. No significant difference was noticed by PD-1, PD-L1 and CTLA-4 expression between PRBC and YWBC. PD-1, PD-L1 expressed on peritumoural lymphocytes and PD-L1 expressed in tumour cells and on intratumoural lymphocytes were suitable to distinguish patient cohorts with different overall (OS)—and disease-free survival (DFS, $p \leq 0.011$ for all comparisons). Higher PD-L1 expression was associated with poor prognosis. PD-L1 expressed on tumour cells represented an independent association with OS (p = 0.023) and DFS (p = 0.032).
Conclusion: Our findings emphasize the relevance of PD-L1 expression in early-onset breast cancer, as an independent negative predictor of prognosis irrespective of pregnancy.

E-PS-02-020

Ki67 and phh3 in phyllodes tumours

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Objective: Phyllodes tumour and fibroadenomas are group of neoplasm consisting of proliferation of both epithelial and stromal component. Fibroadenomas are considered as totally benign lesion, as to phyllodes tumours can be divide into benign, borderline and malignant categories based on histological appearance. Mitotic rate, using pHH3 and Ki67 index could be used to designate this three categories.
Method: The study included 57 phyllodes tumour treated 2008–2016 in Petrov oncology institute. We analyzed a ki67 index and pHH3 + cell count in stromal neoplastic cells in phyllodes tumour per a 1 sq mm sample of histology slide using scanned images and image analysis software.
Results: 30 were classified as benign phyllodes tumours, Ki67 index in was 9.02+/−1.8, phh3 positive cells per 1 mm2 were in 1.6+/−0.74. In 5 borderline cases Ki67 index was 7.0+/−0.32, phh3 0.93+/−0.441/mm2. The rest 23 cases were classified as malignant phyllodes tumours Ki67 index was 29.34+/−4.4, phh3/mm2 8.12+/−2.20. As a control we used usual fibroadenomas and Ki67 index was 8.7+/−2.0, phh3 – 1.1+/−0.49, a bit lower than in benign phyllodes tumours.; 0.93+/−0.441.
Conclusion: In our hand classification phyllodes tumours on three group based on histology appearance, not on IHC markers. Using IHC markers will provide only two-category: benign and malignant.

E-PS-02-021

FOXP3+ Tregs and CD8+ T-cell immune response in early breast carcinoma

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Objective: Objective: The “cancer immunoediting theory” suggests pivotal functions of the immune system during cancer initiation and progression. However, the potential role of FOXP3+ Tregs and CD8+ T-cells in different stages and subtypes of breast carcinoma (BC) has not been fully elucidated, yet. In this study, we investigated the infiltration of stromal FOXP3+ Tregs and CD8+ T-cells in early BC.
Method: Methods: Immunohistochemistry for FOXP3 and CD8 was performed in whole tissue sections of 126 consecutive early BCs (up to pT2N1). FOXP3+ and CD8+ lymphocyte counts were assessed in a standard surface area of the intratumoural stroma, by microscopic counting and by digital image analysis. The results were correlated with the clinicopathological features of the tumours. Data were analyzed by Kruskal–Wallis test and Chi square cross-tabulation.
Results: Results: Tregs and CD8+ T-cells were more abundant in HER2+ (including luminal/HER2+) and triple negative breast carcinomas (TNBC) versus luminal tumours ($p < 0.05$). Moreover, Tregs and CD8+ T-cells were associated with high tumour grade and high Ki-67 index ($p < 0.05$).
Conclusion: Conclusions: TNBC and HER2+ BC are enriched in Tregs and CD8+ T-cells from the early stages of the disease. Manipulations of the functional status of these cell types by immunotherapeutic approaches may prove as effective anticancer strategies.

E-PS-02-022

Pseudoangiomatous stromal hyperplasia of the breast: Report of three cases

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Objective: Pseudoangiomatous stromal hyperplasia (PASH) is a rare benign mesenchymal proliferative lesion of the breast that occurs predominantly in premenopausal women. It can be incidental finding associated with fibrocystic changes, fibroepithelial lesions, gynecomastia and invasive breast carcinoma. We report clinicopathological and immunohistochemical features in three cases of PASH.
Method: Three cases of PASH diagnosed at our institution in period of 3 years were grossly and microscopically analyzed and immunostained with a panel of antibodies: CD31, CD34, CD68, vimentin, actin, EMA, CKAE1/AE3, ER, PR, bcl2 and S-100.
Results: All patients in our study were women aged 17, 39 and 41 years, clinically presented with palpable, mobile, firm mass localized in left breast in two of the cases and in right breast in third case. All patients were treated with surgical excision. Frozen section done in one case was suggestive of benign lesion. Grossly tumours were well circumscribed, rubbery, tan-yellow in color, measuring from 4.5 to 11 cm in greatest dimension. Microscopically, all lesions were composed of complex network of slit-like spaces, lined by spindled cells that resembling vascular spaces, surrounded by dense collagenous stroma. Immunohistochemically stromal celss showed: strong positivity for CD34, vimentin and bcl2; actin was positive in single cells and other markers were negative. There was no reccurence in any of the patients after 12 months follow up period.
Conclusion: PASH as a rare benign entity clinically must be differentiated from fibroepithelial lesions and histologically from low grade angiosarcoma, especially on frozen sections. Follow up after excision is recommended because of reported recurrences.

E-PS-02-023

S100 protein expression in triple negative breast carcinoma

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Objective: S100 protein is strongly expressed in the epithelial cells of typical and atypical microglandular adenosis (MGA and AMGA respectively). There is increasing evidence that MGA and AMGA are precancerous lesions with a possible particular link to triple negative breast carcinoma. The associated carcinoma usually also expresses S100 protein. This study aimed at finding out the incidence of S100 protein expression in a series of triple negative breast carcinomas
Method: Sections of 35 triple negative breast cancers were stained for S100 protein using the immunoperoxidase technique. Sections 0f another 35 cases of breast carcinomas negative for ER and PgR but positive for HER2 were similarly studied as a control group.
Results: S100 protein was expressed in 9/35 (26 %) triple negative carcinomas compared with 1/35 (3 %) ER and PgR negative HER2 positive tumours. The difference was statistically significant ($p < 0.01$). No MGA or AMGA elements were identified in any of the S100 positive carcinomas
Conclusion: In spite of the absence of Identifiable MGA elements, there is a high incidence of S100 protein expression in triple negative breast carcinoma

E-PS-02-024

Invasive breast carcinoma in brazilian young patient: Post-mortem diagnosis

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Objective: Report a case of a young patient with invasive lobular breast carcinoma (ILBC) diagnosed during autopsy.

Method: It was performed an autopsy in an obituary verification service.
Results: Female, 30 years old, black, multiparous, with a posterior thoracic pain, jaundice and choluria 2 weeks before the death. Evolved with fever, thrombocytopenia, worsening jaundice and abdominal pain presenting, in the next day, high gastrointestinal bleeding. Days later, presented intense thirst, profuse sweating, anasarca, hypotension and "gasping" evolving with cardiopulmonary arrest without reversal after resuscitation maneuvers. At autopsy: jaundice, ecchymosis, palpable nodule located in the left breast, pleural effusion, heart petechiae, increased lymph node next to the gallbladder, multiple yellow lesions with hemorrhagic rim on liver and pancreas within the patterns of normality. Pathologic analysis revealed ILBC.
Conclusion: ILBC can affect women at any age, but it's more common as grow older. In autopsy, it was found out that the patient had advanced non-diagnosed IBC, showing the importance of screening exams careful for breast cancer, because she wasn't within the covered age group. This case demonstrates that the age estabilished by the Ministry of Health of Brazil for the screening exams needs to be revaluate.

E-PS-02-025

Different stromal sarcomatous component in malignant phyllodes tumours

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Objective: The aim of study is to estimate stromal sarcomatous component in malignant phyllodes tumours (MPT).
Method: A retrospective review (2008–2016) of clinical dates, pathological and ICH of MPT from 18 patients was carried. Mean age at diagnosis was 53,8 years (from 28 to 87). Size of primary tumours varied from 2 to 23 cm. 8 women suffered from local recurrence (from 1 to 5 times, time interval since ptimary MPT excision: 3–20 months).
Results: In 18 primary MPT squamous metaplasia were find in 4 cases, liposarcoma component –7; chondrosarcoma component –3, fibrosarcomatous stroma –10, rhabdomyosarcoma component –1, osteochondroid metaplasia- 4, multinucleated giant cells –2, pleomorphic sarcomatous component –8. Combination and heterogeneity of intratumoural stomal component was revealed in 13 cases. Recurrence MPT from four patients were multiple histologically different nodes in breast. In 3 cases MPT were associated with carcinoma (2 – RCC, 1 – HCC), in 1 – with angiomyolipoma of kidney. Distant metastasis in 6 cases: to lung (4), to retroperitoneum (1), to ilium bone (1) showed stromal component like pleomorphic sarcoma (3), fibrosarcoma (2), liposarcoma (1).
Conclusion: Heterologous stromal elements were revealed in 8 cases with difference between primary and recurrent MPT in 5 cases.

E-PS-02-026

Assessment of morphology changes in breast cancer in initial, intermediate CNB and in resection specimen after neoadjuvant chemotherapy

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Objective: We performed analysis of histology changes within tumour before, during and after neoadjuvant therapy.
Method: The study included 51 breast carcinomas before, during and after neoadjuvant therapy. We have analyzed histology grade changes before, during (after 2 cycles NCT) and in resection specimen.
Results: The distribution of histology grade in initial biopsy was G1 – 4.08 % (n = 2), G2 – 40.8 % (n = 20), and grade 3–55 % (n = 27). In intermediate CNB after 2 cycles of neoadjuvant therapy we had 15 cases (29 %) with no tumour cells, among them in in 5 cases (10 %) we cannot identify tumour in resection specimen, but in intermediate biopsy we assessed that cases as no adequate samples. Tumour grade in the rest intermediate CNB changed G2 from 40.8 to 68,5 % and G3 from 55 to 20 %. In final resection specimen there was 9 cases (17,64 %) with pCR. Tumour grade in resection was comparative as in initial biopsy and was G1 3 %, G2 – 47 %, G3 – 50 %.
Conclusion: Intermediate biopsy during NCT could be a good tool to control or fix the tumour regression.

E-PS-02-027

Myoepithelium assessment with p63 immunostaining in formalin-fixed paraffin-embedded breast cancer tissue pre-treated with RNA-later

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Objective: To assess myoepithelium with p63 in fresh breast cancer (BC) tissue samples collected in RNA later for further analysis with Next Generation Sequencing (NGS) technique. For a better understanding of the NGS bulk-analysis, a central part of the sample in RNA-later is formalin-fixed paraffin-embedded to score relative cellularity in % on hematoxylin-eosin (HE) staining (% of invasive cancer, cancer in situ, benign epithelium, lymphocytes and fat). Our aim is hence to test p63 immunohistochemistry (IHC) to highlight myoepithelium and to facilitate the evaluation of the relative cellularity on BC-tissue pre-treated with RNA-later.
Method: Two-hundred and twenty-four selected samples of fresh BC tissue collected in RNA-later. A 10 mg central piece from each sample was FFPE and assembled in a tissue-microarray (TMA) and sectioned to HE and p63 IHC.
Results: All samples (n = 224) had internal control for myoepithelium surrounding in situ cancer or benign epithelium. p63 showed positive nuclear staining in myoepithelial cells in 92 % (206/224) of samples and false negative p63 staining in 8 % (18/224).
Conclusion: p63 IHC is assessable in samples of FFPE BC-tissue pre-treated with RNA-later.

E-PS-02-028

Analysis of BMI and pathological response to neoadjuvant chemotherapy in patients with invasive breast carcinomas

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Objective: Obesity at breast cancer diagnosis is associated with inferior survival, including breast cancer-specific survival. The pathologists routinely evaluate the pathologic response to neoadjuvant therapy, since it represents an independent prognostic factor in breast carcinoma. The aim of this study is to assess the association between patient's body mass index (BMI) and the pathologic response to neoadjuvant chemotherapy in invasive breast carcinomas (IBC).
Method: We retrospectively reviewed the IBC identified in the database (2012–2015), diagnosed on tru-cut biopsy and underwent neoadjuvant chemotherapy followed by surgical treatment and processed according to MD Anderson protocol). For comparison, all patients were divided into normal weight (NW) group (BMI < 25 kg/m2), overweight (OW) (BMI 25–29.9 kg/m2) and obesity (OB) group (BMI ≥30 kg/m2) based on the WHO criteria.
Results: 76 patients were identified from which 23 were NW, 27 OW and 26 OB. Out of these 76 cases, 5 cases had complete pathologic response

(1 NW, 1 OW, 3 OB), 36 cases partial pathologic response (11 NW/11 OW/14 OB), and 26 cases no pathologic response to the neoadjuvant chemotherapy (8 NW, 12 OW, 6 OB).
Conclusion: Statistical analysis did not show significant differences between the pathologic response to neoadjuvant chemotherapy in different body mass index groups (0.2028).

E-PS-02-029
Metastases from invasive micropapillary urothelial carcinoma (IPUC) mimicking a unilateral gynecomastia: Case report
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Objective: The IMUC is an uncommon variant of urothelial carcinoma with incidence of 0.7 %, high metastatic potential and poor prognosis.
Method: We report a case of a 55-year-old man diagnosed previously of invasive micropapillary urothelial carcinoma (IMUC). During chemotherapy he present with unilateral "gynecomastia". The clinical examination of the breasts revealed an enlarged and some erythematous right breast. Mammography showed gynecomastia-like features and skin thickness with subcutaneous oedema. An ultrasound-guided core needle biopsy was performed.
Results: Histological examination shows desmoplastic stroma with ducts with infiltration by small clusters of malignant cells floating in empty spaces. The individual tumour cells had abundant eosinophilic cytoplasm and nuclei with irregular distribution of chromatin. Tumours cells showed positive reaction for GATA3, CK 20 and CK7 and negativity for mammoglobin. Podoplanin, CD34 and CD31 positivity from spaces, revealed true vascular invasion. These findings corroborated the diagnosis of breast metastasis from invasive papillary urothelial carcinoma.
Conclusion: Metastatic IMPC of the bladder must be distinguished from MPC of others organs. Immunohistochemistry panel include: GATA3, uroplakin III, CK20, ER, mammaglobin, TTF-1, and CDX2, WT1, Pax8. Metastases to the breast from non-mammary primary tumours are account for 0.5–2.0 %. The most common cancer metastasized to male breast is prostate cancer.

E-PS-02-030
Familiar lesion from somewhere else: Two cases of tubular adenoma of the breast
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Objective: Tubular adenoma is a rare benign tumour of the breast accounting for 0.13–1.7 % of benign breast lesions. Few cases have been reported in the literature especially in reproductive age group. The clinical and imaging features are similar to those of fibroadenomas. We herein describe two rare breast tubular adenomas in 45 and 52 year-old women.
Method: Two women applied with palpable breast lesion lasting for 2 and 3 months, respectively. The laboratory tests were normal and the mammography revealed a 32x19 mm sized mass in the lower outer quadrant of the left breast and 43x15 mm sized mass concordant with fibroadenoma in the upper inner quadrant of the left breast in cases, respectively. The tru-cut biopsies of the lesions were defined as tubular structures generally showing myoepithelial layer in a small amount of fibrotic stroma and excisional biopsy was performed for the accurate diagnosis.
Results: After the excision the two lesions showed similar morphological findinga such as small tubular structures all showing myoepithelial layer highlighted with p63 within very limited stromal component and the lesions were diagnosed as tubular adenomas of the breast
Conclusion: Tubular breast adenomas are rare epithelial tumours considered as variants of pericanalicular fibroadenomas with prominent adenosis-like proliferation. Tubular adenomas are benign lesions with smooth borders in contrast to tubular carcinomas characterized with the lack of myoepithelial layer. These lesions are benign however the limited samples especially in core biopsies confict pathologists' approach and excisional biopsy is required for giving the most accurate diagnosis. This is why it is important to be aware of this kind of epithelial proliferations.

E-PS-02-031
Breast neurofibroma revealing a von Recklingenhausen disease: A case report
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Objective: Neurofibroma that occur in the breast and constitute a revealing signs of the disease at adulthood are extremely rare. We report a case of a 3O-year-old woman presenting a neurofibroma of the breast revealing Neurofibromatosis type 1.
Method: This is a case of a 30-year-old woman with no medical history. She presented with a left breast lump evolving for a year.
Results: The clinical examination revealed multiple café-au-lait spots and a left breast tumour measuring 3 cm in the upper-outer quadrant. The mass was well limited and mobile. The ultrasound demonstrated a 3 cm well-defined, hypoechoic solid mass suggesting fibroadenoma. The mammography was performed and showed the well defined mass. The patient had a lumpectomy. Histopathologic examination of the mass showed benign tumour structure non encapsulated but well circumscribed, measuring 3 cm composed of interlacing bundles of elongated cells with wavy nuclei in the breast tissue areas constituted of lobuli. Several small nerves fibres were also present. Mitotic activity was low. Immunohistochemical examination revealed that tumour cells were S100 protein positive. Actine and CD 34 were negative.
Conclusion: Neurofibromas occurring in the breast are very rare. However, these must be taken into account since they can be revealing signs of the disease. Imagery certainly has an important diagnosis role. MRI remains the favourite diagnosis means to highlight neurofibromas in the breast and to detect a possible malignant transformation. Diagnosis is based on the standard histological and immunohistochemical study especially in atypical forms.

E-PS-02-033
Synchronous encapsulated papillary carcinoma, ductal carcinoma in situ and invasive carcinoma of non-specific subtype in a breast tumour: A rare pathological feature
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Objective: Encapsulated papillary carcinoma (EPC) represents <1 % of breast carcinomas. This lesion is typically indolent but may rarely have synchronous invasive lesions. This report aims to describe clinical and histopathological features of this tumour and highlights the pathologist's role in establishing the right diagnosis.
Method: We describe a case of EPC associated to both ductal carcinoma in situ (DCIS) and invasive carcinoma of non-specific subtype (ICNSS) diagnosed in pathology and gynecology departments
Results: A 49-year-old-woman presented with a right breast lump. Physical examination found a-1 cm-firm-nodule occupying the upper-outer-quadrant of the right breast. Mammography and ultrasonography revealed a well-circumscribed hypo-echoic mass measuring 1 x 1 x 0,8 cm devoid of micro-calcifications graded with Breast Imaging-Reporting and Data System (BI-RADS) as class 4. DCIS of intermediate grade with a focus of

ICNSS were found on core- needle-biopsy. Breast conservative surgery with lymphadenectomy was performed. Gross-examination revealed a 1 cm-well-circumscribed-white-tumour. The tumour corresponded histologically to an EPC with DCIS and ICNSS without lymph node involvement. The lack of immunohistochemical staining with myo-epithelial markers confirmed the diagnosis of EPC.
Conclusion: EPC is a rare entity. Immunohistochemistry is mandatory to rule out other papillary-breast-lesions. Extensive specimen sampling is crucial to not misdiagnose associated invasive carcinoma.

E-PS-02-034
CK7-negative metastatic breast carcinoma in axillary lymph nodes, with no clinical evidence of a primary carcinoma (occult breast cancer)
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Objective: To present a CK7-negative metastatic breast carcinoma in axillary lymph nodes, with no clinical or radiographical evidence of a primary tumour.
Method: A 63yo female patient presented with subcutaneous mass of the right axilla. Surgical removal of the mass revealed two brownish nodules, measuring 6,5X5X3cm and 5X3X1cm.
Results: Microscopic examination revealed lymph nodes with metastatic infiltration of medium-high grade adenocarcinoma. Immunohistochemisty was positive for CKAE1/AE3, CK8/18, ER, PgR, GCDFP-15 and mammaglobin and negative for CK7, CK20, CK5/6, CD10, TTF-1, Synaptophysin and ChromograninA. Based on these findings, the most likely diagnosis was metastasis from a primary breast carcinoma. We advised further diagnostic evaluation of the patient but primary breast tumour was not detected by any other examination.
Conclusion: Occult breast carcinoma presents through regional nodal or distant disease, without clinical or mammographic evidence of a primary tumour. Its incidence is 0.3–1 % of all newly diagnosed breast cancers. The site of detected disease is almost always an axillary lymph node. Reported cases of CK7-negative breast carcinomas are usually neuroendocrine in differentiation. Differential diagnosis should be made from an adenocarcinoma of cutaneous eccrine glands with apocrine features. Although immunohistochemistry is not always conclusive, breast carcinoma remains the most possible diagnosis, unless proven otherwise.

E-PS-02-035
Osteosarcoma or osseal metaplasia of the breast?
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Objective: Primary osteosarcoma is a rare breast soft-tissue tumour. Osteosarcomas of the breast may arise either from pre-existing benign or malignant phyllodes tumour or from previously normal breast tissue. Because of the rarity of the disease, optimal treatment are still to be defined.
Method: A 50-year-old women with no other comorbid illnesses was presented to our center for further evaluation of a painless hard lump in left breast. Her past, medical and family histories were unremarkable in this moment for us. She had clinical examination, diagnostic mammography and laboratory findings. Macroscopic examination of the surgical specimen revealed a well-circumscribed tumour with areas of calcification.
Results: Our patohistological diagnosis was primary osteosarcoma of the breast. Second opinion was osseal metaplasia, and third nonconventional opinion did not confirme either diagnosis. Later, after our diagnosis of osteosarcoma, we get a history of the existence of abnormalities in her skeletal system in a greater number of phalanges of the foot. No evidence of disease after 13 months.
Conclusion: Open question still stands: Is it osteosarcoma or osseal metaplasia?

E-PS-02-036
Metaplastic carcinoma of the breast; A case report
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Objective: Metaplastic carcinoma of the breast(MCB) is a rare subtype of invasive breast carcinoma that tends to have an aggressive clinical-presentation and variety of distinct histological designations.
Method: A 75-year-old female was admitted to the hospital with a 2-year-history of a palpable mass in right-breast. Ultrasonographic examination revealed a 8 cm solid mass and no axillary lymph-nodes.
Results: In histopathological evaluation of the trucut biopsy a quite atypical mesenchymal tumour was seen. The tumour in the mastectomy material was consisting of mesenchymal cells with high mitotic activity, high nucleer-grade and wide necrosis. Very small areas of glandular differentiation of epithelial component, osseos and chondroid metaplasias were observed in serial-sections. Immunohistochemically Vimentin and CD10 were diffuse positive in sarkomatoid component, but Desmin, Smooth-Muscle-Actin(SMA), Cytokeratins, p63, Epithelial-Membrane-antigene(EMA),S100,CD34, Estrogen, Progesterone and HER2-protein were negative. Ki67 index was 80 %.This tumour was diagnosed as MCB(high grade sarcomatous carcinoma with osseous and chondroid metaplasias). Postoperative chemotherapy was applied; however the tumour recurred locally in the fifth-month.
Conclusion: MBC represents 1 % of all breast cancers diagnosed annually. It has a suboptimal response to standard chemoterapy regimens and characteristically poor prognosis. So it is important to diagnose it soon in order to provide the patient longer survival.

E-PS-02-037
Immunohistochemical analysis of fascin, steroid receptors, and HER-2 overexpression in invasive ductal carcinoma of breast and its implications for prognosis
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Objective: Fascin, an actin cross-binding protein, is a critical element in cell motility. Overexpression of fascin mediates epithelial-mesenchymal transition and aggressive behaviors of invasive cancer, but its role in therapeutic and prognostic significance has yet to be established. Expression of fascin was analyzed in 107 Asian female with invasive ductal carcinoma of breast (IDCB) and compared to not only expression of estrogen receptors (ER), progesterone receptors (PR), and HER-2 but also to clinical parameters such as size, lymph node (LN) status, and metastasis.
Method: Tissue microarray was formulated from well-preserved paraffin embedded tissues of 107 female with IDCB. Immunohistochemical analysis of fascin, ER, PR, and HER-2 expression was performed to identify its correlations with clinical parameters. Chi-square test was employed with a significance of p-value <0.05.
Results: Expression of fascin was observed in 21.5 % and correlated with ER negativity ($p = 0.001$), PR negativity ($p = 0.019$), and triple negativity ($p = 0.001$). Correlation between fascin overexpression and clinical parameters such as age, grade, size, and stage was statistically insignificant, whereas fascin overexpression showed positive associations with LN metastasis

Conclusion: These results suggest that overexpresssion of fascin may contribute to more aggressive behaviors of cancer and represent a potential target for therapy in ER/PR negative breast cancer

E-PS-02-038

Expressions of estrogen receptor, HER-2, Bcl2 and CyclinD1 in invasive ductal carcinoma of the breast and comparison with the clinical- histopathological parameters

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Objective: Invasive Ductal carcinoma(IDC), the most common type of breast cancer, is a heterogeneous tumour which has many variations in morphological, molecular features, clinical course and treatment response. So it is important to determine the exact prognostic factors to provide the patients appropriate treatment approach.
Method: The aim of this study was to assess immunohistochemical expressions of Estrogen Receptor(ER), HER-2, Bcl2 and CyclinD1 in 70 patients with IDC and compare them with the clinical-histopathological parameters in order to determine the prognostic significance of them. This study was supported by a project from the Scientific Research Projects Management Unit of Mugla Sıtkı Kocman University (Grant number: 16/086).
Results: Fifty percent of the ER-negative tumours were Bcl2-positive. Among these Bcl2-positive tumours; the ratio of vascular-invasion, axillary lymph-node metastasis, distant-organ metastasis, HER2 positivity, presence of in-situ-carcinoma were 20 , 20 , 0 , 20 and 20 % respectively. 41.6 % of the ER-negative tumours were CyclinD1-positive. Among these CyclinD1-positive tumours; the ratio of vascular-invasion, axillary lymph-node metastasis, distant-organ metastasis, HER2 positivity, presence of in-situ-carcinoma were 16.6 , 16.6 , 0 , 33.3 and 33.3 % respectively.
Conclusion: These findings indicate that Bcl2 and CyclinD1 expressions favour better clinical course with lesser vascular-invasion, lymph-node/distant-organ metastasis, HER2 positivity and presence of in-situ-carcinoma.

E-PS-02-039

Can morphological and molecular parameters of the primary breast tumour predict the status of non-sentinel lymph nodes after positive sentinel lymph node on core biopsy?

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Objective: Axillary lymph node status is the main prognostic factor in breast cancer patients. Sentinel lymph node (SLN) biopsy is the gold standard in evaluation of the axilla. From a standard point of view, axillary clearance is required, however, in cases of SLN micrometastasis or when criteria for Z0011 are met, no further surgery is needed. We are aiming to evaluate which morphological/molecular parameters of the primary breast tumour could predict the positivity of non-SLN.
Method: A retrospective study was performed on 170 consecutive patients (2012–2016), diagnosed with invasive breast carcinoma, in which cases SLN biopsy was performed for staging.
Results: In 42 (24 %) cases the SLN presented metastases, out of which 11 cases with micrometastasis and 6 cases met the Z0011 criteria. 25 patients subsequently underwent axillary LN dissection but only 28 % (7 cases) had positive non-SLN. In this series, the histological type ($p = 0.78$), grade ($p = 0,97$), tumour diameter ($p = 0.05$), patient's age ($p = 0.35$), number of positive SLN ($p = 0.35$), presence of extracapsular extension ($p = 0.6$), molecular profile ($p = 0.36$) do not statistically influence the positivity of the non-SLN.
Conclusion: In our series the histological/molecular parameters cannot predict the positivity of non-SLN. In these particular cases, axillary lymph node dissection will remain the surgical treatment to choose.

E-PS-02-040

Three cases of breast carcinoma with osteoclastic multinucleated giant cells: Clinicopathological and imunohistochemical study of osteoclastic multinucleated giant cells

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Objective: Carcinoma with osteoclast-like giant cells (OCGS)represents a unique type of breast neoplasm, characterized by the presence of multinucleated OCGS, and comprises of less than 2 % of breast carcinoma. OCGS are a rare phenomenon. Origin of OCGS remains controversial.
Method: We report a study of 3 patients with invasive carcinoma, in which the OCGS were present, despite different histological morphology of tumours. A 67 year old woman (Case 1) had the OCGS accompanying invasive mucinous carcinoma, a 71 year old woman (Case2) with metaplastic carcinoma with chondroosseal differentiation, and a 71 year old woman (Case 3) with carcinoma with choriocarcinomatous features. These cases had been collected from CGB s.a. laboratory and from the Department of pathology Faculty hospital Ostrava.The OCGS were evaluated with immunohistochemistry, using antibodies directed against CD68, CK AE1/AE3, Faktor VIII, Ki67.The OCGS were counted in high-power fields.The distribution pattern of the OCGS was assessed.
Results: By imunohistochemistry the OCGS expressed histiocyte marker CD68 in all three cases. Faktor VIII and epithelial marker(CKAE1/AE3)was lost in all of the cases examined.
Conclusion: The results indicate a pathogenesis of the OCGS. The OCGS derive from macrophages responding to hypervascular stroma with secretion of cytokines, induced by breast cancer.

E-PS-02-041

TP53 mutation in triple negative breast cancer

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Objective: Triple-negative breast cancer (TNBC), a heterogeneous disease, generally has poor prognosis. One molecular alteration that occurs in the majority of TNBC is mutation of tumour suppressor gene TP53. Mutant p53 has been recognized to influence response to chemotherapy.
Method: A series of 35 patients with triple negative breast cancer (ER-, PR-, and HER2-) diagnosed in 2013–2016, hospitalized at Theageneion Cancer Hospital was analyzed. Tissue samples were stained with H & E to determine the histopathological type of patients' tumours. Nuclear p53 protein levels were also determined in tissue samples by immunohistochemistry (IHC) using DO-7 anti-p53 antibody.
Results: Tumours were variants of breast carcinomas comprising of invasive ductal carcinoma (NST) (74,2 %), apocrine (11,4 %), lobular (5,7 %), medullary (2,8 %) and metaplastic (5,6 %) carcinoma. The cellular immunoreaction of the tissue samples was evaluated based on the intensity of the specific nuclear staining. In our study, positive p53 (only moderate or strong staining) nuclear immunostaining was found in 22 tumours (62,8 %) versus 13 negative tumours (37,1 %).
Conclusion: Throughout this study, we posed some questions. Can we use immunohistochemistry to evaluate mutant (missense and nonsense mutations) p53 in routine practice? Does mutant p53 increase or decrease sensitivity to chemotherapy?

E-PS-02-042

Immunohistochemical evaluation and prognostic value of GATA-3 protein in breast cancer

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Objective: The aim of this study is the immunohistochemical evaluation of the prognostic value of the nuclear marker GATA-3 in breast cancer tissues, and also to correlate its expression with clinicopathological parameters. Breast cancer is considered the most frequently diagnosed cancer in females, accounting for almost 23 % of all cancer cases. GATA-3 is a marker of significant prognostic value, although its role in various cancer subtypes still remains unclear.
Method: The sample pool was comprised of 55 patients with breast carcinoma of various subtypes. In these samples, we conducted an immunohistochemical analysis using anti-GATA-3 antibody in order to evaluate its expression in correlation with various clinicohistopathological parameters.
Results: There was no statistically significant relationship of GATA-3 expression with age, gender, differentiation, lymph node invasion, type of tumour and PR or HER2 positivity. However, there was a strong statistically significant relationship with Estrogen Receptor positivity ($p < 0.0001$).
Conclusion: In conclusion GATA-3 can be used as an efficient prognostic marker for breast cancer, especially for ER-positive carcinomas and can potentially be used as a drug target. However due to the limited number of cases used in this preliminary study, further analysis is necessary in order to establish these results.

E-PS-02-043

Breast metastasis from cutaneous melanoma: A case report and review of the literature

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Objective: Breast metastases are very uncommon, either from solid tumours or malignant melanoma. Melanoma is, however, among the most commonly reported primary tumours to metastasize to the breast.Approximately 20 % of malignant melanomas will metastasize, whether by hematogenous or lymphatic route. The incidence of breast metastases from extramammary tumours varies between 1.3 and 2.7 %.
Method: We present the case of a 57-year-old woman with history cutaneous melanoma of the foot. She presented with a palpable lump in the the upper inner quadrant of the right breast.
Results: Core needle biopsy of the breast showed breast parenchyma with a solid appearing cellular infiltrate composed of large epithelioid cells with prominent nucleoli and ample eosinophilic cytoplasm. Intra and extra cellular pigmentation were observed. The tumour cells showed strong and diffuse staining for S100 melan-A and HMB45 establishing their melanocytic lineage
Conclusion: Metastases to the breast from melanoma are uncommon but should be suspected in patients with a breast mass and a prior history of melanoma even years after a primary has been removed

E-PS-02-044

Molecular and biological features of the metaplastic carcinoma of the breast

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Objective: Metaplastic carcinoma of the breast is a tumour with metaplastic components (squamous, glandular, spindle) or with features of the high grade mesenchimal tumour.
Method: We analyzed 5 cases of metaplastic carcinoma of the breast (2009–2016). Mean age of female patients was 53 years.
Results: Observed metaplastic carcinomas had variable histological structures: solid areas composed of large dark cells alternated with small tubular structures. Tumours consisted of epithelial and mesenchimal components. Immunohistochemical study showed pronounced expression of pancytokeratin, CK 7 and 20 by tubular structures. Tumour cells expressed CK5/6 and vimentin, which is attributed to tumours with squamous and mesenchimal differentiation. This is a result of transition of mesenchimal component to squamous. Epithelial component showed pronounced expression of E-cadherin, which suggests high adhesive potential of tumour cells. For epithelial structures index Ki-67 was more than 45 %.
Conclusion: Metaplastic carcinoma of the breast is a rare tumour characterized by presence of epithelial and mesenchimal components. Epithelial component has a complex dimorphic origin as a result of transdifferentiation. High adhesive potential and proliferative capacity allow to assume that these tumours are aggressive with propensity for fast growth and recurrence.

E-PS-02-045

Intratumoural heterogeneity in breast cancer

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Objective: The aim of study is to examine intratumoural heterogeneity in breast cancer.
Method: We have assessed the specimens of 160 patients (age 18–73) with breast cancer T1-4 N0-2 M0-1. Immunohistochemical study with antibodies to estrogen receptor (ER), progesterone receptor (PgR), Ki 67, Bcl-2, Her2, p63, smooth muscle actin, cytokeratin 7, vimentin, E-cadgerin (Dako, Lab Vision Flex) was performed.
Results: Invasive carcinomas of no special type (IC NST) compose the main bulk of breast cancer (up to 75 % of all cases). Expression of Her2, ER and PgR is variable within a tumour. Intratumoural morphological heterogeneity of ICNST manifests by presence of 5 different structures: tubular, solid, alveolar, trabecular and discrete nests of tumour cells. These cells have a full set of molecules for establishment of intercellular contacts (cadherin-catenin complex and integrins β1), as well as integrin receptors for contacts with connective tissue. In second subtype with solid and alveolar structures most of the cancer cells don't have connections with stroma, except for the outer layer of cells. Cancer cells of these structures express cadherin-catenin complex, but they don't possess integrin receptors. Triple negative tumours often consist of one type of morphological structures. Luminal breast cancer mostly contains 5 types of structures.
Conclusion: Connection between intratumoural morphological heterogeneity and molecular subtypes was established.

E-PS-02-046

Breast solid papillary carcinoma, a distinctive form of papillary carcinoma - report of 2 cases

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Objective: Carcinomas with papillary architecture encompass conventional papillary carcinoma, intraductal papillary carcinoma, encapsulated papillary carcinoma and papillomas with ductal carcinoma in situ. Solid

papillary carcinoma is uncommon (<1 % of breast carcinomas), and raises problems in diagnosis.
Method: Patients were 68 and 46 years-old females with right breasts tumours measuring 10 mm and 45 mm respectively.
Results: Microscopically tumours were similar, composed of multiple large distended nests in a "geographic" pattern, of homogeneous and cohesive cell proliferation, with delicate fibrovascular cores. Extracellular mucin was present focally. Tumours were grade 2 (Elston & Ellis classification). Immunohistochemistry revealed neuroendocrine differentiation. The invasive character was establish as some of the nests were negative for myoepithelial stains. No invasive carcinoma NST was observed. Sentinel lymph nodes were negative.
Conclusion: Solid papillary carcinoma is a distinctive form of papillary carcinoma that raises problem in diagnosis, even so, they present distinctive findings that permits its recognition. The invasion in a blunt manner is many times under evaluated by pathologists and immunohistochemical stains can help as invasive areas lacks myoephitelial cells.

E-PS-02-047
Sentinel Node (SN) macrometastases in Ductal Carcinoma in Situ (DCIS) detected by OSNA assay (One Step Nucleic Acid Amplification)
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Objective: DCIS are unable to metastasise by definition; therefore, the examination of SN only is recommended for largeror higher grade lesions. We present a case of DCIS with metastatic SN identified by OSNA, by detecting CK19mRNA copy number, thus allowing discrimination of macrometastases (CK19mRNA copy number >5000) from micrometastases (CK19mRNA copy number >250but <5000).
Method: DCIS was diagnosed on core needle biopsy (11G)and myoepithelial markers (s.m. myosin and p-63) confirmed thelack of invasive features. SN was submitted to OSNA and an imprint citology, stained with haematoxylin-eosin, was peformed before the molecular analysis. A quadrantectomy was performed.
Results: OSNA of SN was positive for macrometastases (CKcopy number = 690.000) and imprint cytology showed severalclusters of atypical epithelial cells. Morphologically, several foci of DCIS were identified in the surgical specimen but stromal invasion could not be detected, notwithstanding extensive sampling (25 tissue blocks) and the support of immunohistochemical stains for myoepithelial markers. Non SNs were metastases free.
Conclusion: • Metastatic SN may seldom be identified by OSNA and cytology in patients harbouring DCIS • Extensive tissue sampling, morphological examination and immunohistochemistry may be insufficient to detect minimal foci of stromal invasion • The use of complete axillary dissection in such cases is still debatable.

E-PS-02-048
Giant hamartoma of the breast: Case report
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Objective: Breast hamartoma is a rare entity with an incidence of approximately 0.7 % of benign breast masses. Hamartomas may become large and cause breast asymmetry and may imitate malignancy.
Method: A 52 year old female was admitted to the our hospital with a palpable mass at the junction of the outer quadrants of the right breast.
Results: A physical examination revealed a round mass of 4 cm in diameter. There was no axillar lymphadenopathy. No palpable masses of the contralateral breast were detected. The ultrasonography of the lesion revealed a solid, heterogeneous echogenic mass with smooth margins, BIRADS 3/4. A tumourectomy was performed on the right breast. Macroscopically, we find tumour node 9x6x4,5 cm, greyish white colored, oval shaped and encapsulated. Histopathologically, the tumour consisted of mammary glandular tissue in hyalinized fibrous stroma, interspersed with islands of mature fatty tissue. All lobules were structurally normal. Cystic ducts with apocrine metaplasia were evident in specific areas as fibrocystic changes. The lesion was well defined and had a pseudocapsule of compressed adjacent breast tissue. This case was diagnosed: Breast hamartoma (fibroadenolipoma). Fifteen months after the surgery, the patient was with no recurrence.
Conclusion: Surgical resection is the best method of choice for the treatment of breast hamartomas.

E-PS-02-049
Phyllodes tumours of the breast : A clinico-pathologic study of 15 cases
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Objective: To review the clinico-pathological features of phyllodes tumours of the breast.
Method: We retrospectively reviewed the clinical and pathological data of 15 women with histologically proved phyllodes tumours of the breast collected between 2011 and 2016.
Results: All the patients were females. The mean age was 43.6 years (25–71). Eleven patients (73.3 %) were premenopausal. The median tumour size was 6.7 cm (2–22 cm). Histologically, five patients (33.3 %) presented with benign, 1 (6.7 %) with borderline and 9 (60 %) with malignant phyllodes tumours. One malignant phyllodes tumour had an heterologous liposarcomatous element. Six patients (40 %) underwent mastectomy (all cases were malignant phyllodes) and 9 (60 %) underwent conservative surgery (5 benign, 1 borderline and 3 malignant). Thirteen cases (86.7 %) presented negative margins. None had lymph node metastasis. One patient with a malignant phyllodes tumour developed local recurrence after 5 months. Two patients with malignant phyllodes tumours developed distant metastasis (respectively in the liver and in the lung).
Conclusion: In summary, phyllodes tumours are rare fibroepithelial neoplasms with potential for local recurrence and distant metastasis. Histologic classification into benign, borderline and malignant is challenging in some cases and does not correlate well with biological behavior.

E-PS-02-052
Uses of biomarkers in breast cancer: Prediction, prognosis and therapy
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Objective: In order to reveal the prognostics of breast cancer, adapt the treatment and to make it personalized to each patient a molecular classification defined by immunohistochemical (PR, ER, ki67 and HER-2) hormone receptor markers and gene expression signatures are needed. It's has shown a clear relation between prognosis and treatment efficiency. We focused on the association between morphological and molecular aspects in breast cancer patients and bring to light the factors influencing the prognosis and survival of those patients.
Method: A retrospective study was made on 6 years from 2008 to 2014 covering all breast cancer cases hospitalized and diagnosed in pathological anatomy department to obtain Clinical and pathological information.

Immunohistochemical study and histological classification were used to classify breast cancer and to estimate the associations between risk factors and tumour prognostic subtypes.
Results: Of the 631 breast cancer patients included, 9 % were HER-2, 13.80 % were Basal Like, 21 % were Luminal A and 56 % were Luminal B as the most frequency subtype with the most aggressive histopathological characteristics. We were able to demonstrate after a multivariate analysis that: Type of specimen, lymph node invasion, estrogen receptor expression profile, molecular type as well as the initial clinical stage cTNM Represent prognostic factors.
Conclusion: Using the molecular classification we have indicate that the most frequency subtype is Luminal B, we have also demonstrate that clinical and pathological characteristics are associated with prognostic tumour subtypes.

E-PS-02-053
Metastasis of synchronous bilateral breast cancer in gastrointestinal stromal tumour - an extremely rare case
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Objective: The occurrence of synchronous or metachronous malignant epithelial and mesenchymal tumours is rare. Infiltrating ductal breast cancer rarely produces metastasis in the gastrointestinal tract, and when it does it represents a significant differential diagnostic problem. Morphologically they can mimic primary cancers localized in the gastrointestinal tract or peritoneum.
Method: In this paper we showed a female patient with primary, synchronous bilateral breast cancer, which after 5 years of follow-up had given metastases to the lungs, bones, peritoneum and mesentery, and in a node localized in the small intestine. The node was built of two malignant components, mesenchymal and epithelial. Mesenchymal component had histologic and immunophenotypic characteristics of gastrointestinal stromal tumour and epithelial component was morphologically and immunohistochemically identical to the diagnosed primary breast cancer.
Results: Because of all this, the nodal tumour mass was interpreted as a primary gastrointestinal stromal tumour of the small intestine, in which the deposit of metastatic ductal breast carcinoma was observed.
Conclusion: Metastasis of breast cancer in organs of the gastrointestinal tract are encountered rarely, mainly in the terminal stage of the disease. In available literature, a case of metastasis of breast cancer (metastasis of malignant epithelial tumours) in gastrointestinal stromal tumour has not been found.

E-PS-02-055
Xanthogranulomatous mastitis: A case report
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Objective: Xanthogranulomatous inflammation is a rare clinicopathological condition involving many organ systems. Xanthogranulomatous mastitis is an uncommon finding in the breast.The etiology of xanthogranulomatous mastitis is unclear.
Method: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 47 year old woman presented with a palpable mass in the left breast. Breast ultrasound images revealed heterogeneously hypoechoic collection, consistent with BI-RADS grade 3. Lumpectomy was performed. Macroscopically, resection material was firm in consistency, and a 4x4 cm ill-defined lobulated mass-like lesion was found on sectioning. On microscopic examination there was granulomatous inflammation rich in xanthomatous macrophages with widespread areas abscess formation. Ductal ectasia was present. The xanthoma cells showed diffuse cytoplasmic staining for CD68 and were negative for GCDFP15.
Conclusion: The proposed causes of xanthogranulomatous inflammation include obstruction, hemorrhage, inflammation, and local hypoxia. In our case, xanthogranulomatous inflammation may be devoloped secondary to rupture of ectatic ducts. Breast involvement seen with this inflammation has been limited to only few rare cases of mastitis. We would like to report an unusual involvement of this inflammatory process.

E-PS-02-057
Pseudoangiomatous stromal hyperplasia with multinucleated giant cells and gynecomastia - a case report
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Objective: PASH is a benign mesenchymal proliferative lesion of the breast, more frequent in women, but also occurring in men with gynecomastia. The exact etiology and pathogenesis of PASH is not well known. PASH with stromal multinucleated giant cells (MGC) and gynecomastia was described in patients with neurofibromatosis type 1 (NF-1). We describe a case of PASH with MGC and gynecomastia in a male without NF-1.
Method: Seventeen years old men with a left breast mass. A simple mastectomy was performed. The mass weight 131gr and measured 10x6x3cm.
Results: Histology revealed a diffuse stromal myofibroblastic proliferation with irregular anastomosing slit-like pseudovascular spaces, lined by spindle cells. MGC were seen lining the spaces and in the stroma. The background consisted of gynecomastia with epithelial proliferation. Spindle cells and MGC were CD34+, VIMENTIN+, SMA-, D2-40-, RE-, RP-
Conclusion: PASH with gynecomastia is a frequent finding (47,4 %). The presence of multinucleated giant cells is rare and was reported associated with NF-1. In our case that association was not found. The current treatment of PASH is excision with adequate margins, as recurrence is more likely to occur if incompletely excised.

E-PS-02-059
Metaplastic carcinoma (carcinosarcoma) of the breast: A case report
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Objective: Metaplastic breast carcinoma (MBC) is a rare malignancy and accounting for less than 1 % of all breast carcinomas, which is often composed of epithelial and mesenchymal components. This communication highlights a case of this rare tumour and its histopathological and prognostic features.
Method: We report a case of a (MBC) with extensive chondroid differentiation.
Results: An 80-year-old female presented with a three centimeters mass to her left breast. Ultrasound and mammography classified the lesion BI-RADS 5. Microbiopsy showed a tumour composed of interlacing bundles of pleomorphic, spindle shaped cells, with large pleomorphic hyperchromatic nucleus and abundant cytoplasm with frequent mitosis. Amidst these tumour cells, there were irregular clusters of large polygonal to pleomorphic tumour cells with cytoplasmic keratinisation. There were also round to polygonal cells arranged in irregular sheets and occasional ductal pattern. The stroma showed extensive areas of chondroid and osseous diffentiation.

Conclusion: MBC is a rare and aggressive type of invasive breast cancer. As it encompasses a variety of distinct histopathologic designations, diagnostic challenges abound.

E-PS-02-061

Perpendicular inked-margins versus tangential shaved-margins for assessing margin involvement by breast cancer

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Objective: Only a few previous studies have compared the two method of margin assessment, perpendicular inked-margins versus tangential shaved-margins. The effectiveness of intraoperative margin assessments using frozen section also remains to be determined.
Method: This study included 36 wide local excisions of breast carcinomas. We changed protocol for margin evaluation from perpendicular inked margins (Group A, $n = 18$) to tangential shaved margins (Group B, $n = 18$) during a 1.5 year-period. While the specimens were fixed by ordinary method in Group A, the specimens were fixed by polygonal method in Group B. In Group A, margins were classified as positive, close and negative. In Group B, shaved margins were classified positive or negative. And in Group B if shaved margin was considered positive, we reviewed the intraoperative frozen diagnosis.
Results: The rate of "positive" margins was significantly higher in Group B than in Group A: 2 of 18(11 %) versus 8 of 18 (44 %). But when both "positive" and "close" were judged as positive in Group A, there was no significant difference between the two Groups. In Group A, many ventral/dorsal margin were positive, but they were originally classified as positive lateral margins, due to flattening of specimen.Among the cases with positive shaved margin (Group B, $n = 8$), 4 cases had "positive" and the remaining 4 cases were "negative" margins at intraoperative frozen diagnosis.
Conclusion: The tangential shaved-margin technique results in a higher positive rate than perpendicular inked margin technique, suggesting higher sensitivity for margin involvement by cancer. Intraoperative margin assessment was not effective.

E-PS-02-063

Triple negative breast cancers: PDL1 expression in neoplastic and inflammatory cells

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Objective: The Programmed cell death protein1/Programmed cell death protein ligand1 (PD1/PDL1) axis plays an important role on inflammatory response to tumour cells. We investigated PDL1 expression, a potential biomarker for a potential therapeutic strategy, in Triple Negative Breast Cancer (TNBC).
Method: PDL1 immunohistochemistry (Clone CAL10, Biocare Medical) was performed on TNBC cases.Membranous and cytoplasmic expression were considered and assessed not only in neoplastic cells but also lymphocytes in the stroma. Groups and cut-off values for PDL1 expression were 0(0 %), 1(1–10 %), 2(11–49 %), and 3(50 % and above).
Results: We evaluated PDL1 expression in 49 patients, whose mean age was 51.9.Diagnosis were ductal carcinoma($n = 19$),medullary carcinoma($n = 22$),metaplastic carcinoma ($n = 6$),and basal like carcinoma ($n = 2$).PDL1 expression in neoplastic compartment was 1 % and above in 51%of patients, however expression in lymphocytic compartment was 1 % and above in 63.2 %. Scores of peritumoural lymphocytic response were correlated with PDL1 expression in neoplastic cells (rho = 0.42, $p < 0.01$). There was not statistically significant correlation between PDL1 expression and other prognostic parameters (age,diagnosis,histological grade, stage,lymphovascular/perineural invasion,overall survival).
Conclusion: Further investigation is needed to understand the role of PDL1 expression in TNBCs more clearly.

E-PS-03 Cardiovascular Pathology

E-PS-03-001

Extramedullary haematopoiesis in a healing myocardial infarct: A commonly overlooked histopathological feature

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Objective: This case report aims to highlight the existence of extramedullary haematopoiesis in the context of acute myocardial infarction, and empower pathologists in reporting such findings in myocardial specimens.
Method: The patient is a 54 year old Indian male who underwent left ventricular assist device (LVAD) application due to end stage ischaemic cardiomyopathy. The left ventricular apex removed during the application of the LVAD was sent to the pathology laboratory for evaluation.
Results: Histologically, the specimen showed features of acute, recurrent and chronic myocardial ischemia. Areas of coagulative necrosis were seen, surrounded by granulation tissue and fibrosis. Contraction band necrosis was also noted. Additionally, multiple foci of extramedullary haematopoiesis was seen congregating around the infarcted areas. These cells were confirmed with immunohistochemistry (CD61, CD71, CD117, CD34 and myeloperoxidase), where the main precursors were from the erythrocyte and the myelocyte lineage, with a rare megakaryocyte precursor noted.
Conclusion: As the demand for histopathological analysis of myocardial specimens increases, a pathologist should be well acquainted with commonly encountered conditions. EMH is an abnormal process that is mostly associated with haematological malignancies when it occurs outside the liver and the spleen. However, in the context of a recent myocardial infarction, it is prudent to note its likely benign nature; whereby its presence is probably due to the attraction of peripheral blood stem cells by the underlying inflammatory process.

E-PS-03-003

Sudden cardiac death in calcific aortic stenosis

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Objective: The underlying diseases for sudden cardiac deaths are in non-forensic cases not well studied, as autopsy rates plateaued at lowest level since decades. Even if relatives of the deceased agreed on an autopsy, the underlying pathology is seldomly revealed on postmortem examination. Aortic stenosis is rarely considered within the differential diagnosis.
Method: The autopsy databases of two different pathology departments were searched for sudden death cases which were associated with calcific aortic stenosis.
Results: Within a period of 2 years (2015–2016) were two cases identified. In both cases was the heart of the deceased thoroughly investigated and multiple tissue samples were submitted. Within the tissue samples which were submitted from the aortic valve annulus were calcific masses present, which extended to and into the AV-node. Surrounding the calcific deposits was an in part pronounced inflammatory reaction.

Conclusion: Conduction system should be thoroughly investigated in cases of calcific aortic valve stenosis. The results warrant further investigation in this field.

E-PS-03-005

Histopathological differences between hypertrophic and dilated cardiomyopathy

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Objective: Hypertrophic Cardiomyopathy (HCM) is an inherited disorder characterized by the presence of increased left ventricular wall thickness. Dilated Cardiomyopathy (DCM) develops when the ventricles enlarge and weaken causing contractile dysfunction of the cardiac muscle.
Method: In order to define the HCM-DCM differences, histological and immunohistochemical examination of left ventricular tissue fragments was performed. The stains used for histological examination were Hematoxylin&Eosin and Masson's Trichrome(TRI), whereas the antibodies used for the immunohistochemical study were Anti-Desmin, Anti-CD34, Anti-Collagen I and Anti-TnT.
Results: H&E staining in DCM revealed slightly enlarged or wavy, elongated muscle fibers with hypochromatic, heterogeneous vascular sarcoplasm, by a decrease of myofibril numbers. In HCM myofibrillar disarray and disorganization were observed, combined with myocytes enlargement and hyperchromatic nuclei. Immunohistochemical expression and staining patterns of the markers Desmin, TnT and CD34 confirmed the above findings, with CD34 being a specific diagnostic marker for DCM. TRI and H&E indicated in both CMPs dense collagen fibrils with the interstitial tissue in DCMto be quadrupled. Immunostaining with Col I corroborated this increased fibrotic process.
Conclusion: Numerous features differentiate DCM from HCM with myocardial size and architecture being predominant. Interstitial fibrosis in DCM surrounds and isolates myocytes, while in HCM forms foci. DCM also increases T-lymphocytes number.

E-PS-03-006

On pathological neuro-vascular factors of idiopathic and renal hypertension

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Objective: Since discovery of blood circulation (HARVEY 1628), homoeostasis of blood-pressure (CANNON) & blood volume (GAUER) are till today genuine and renal hypertension pathogenesis incl. apoplexy cerebri (HIPPOCRATES) not clarified.
Method: Vascular motor activity, rat-blood-pressure = BP. Ref.: 1. author. **Handout:**
Results: Isolated prep.: Angiotensin-II/5-HT/PGs/vasopressin = VP & K+ induce spontaneous-phasic (SPC:0.5–2/min) in rat portal/human renal veins (high sensitivity to Angiotensin-II-contr. to 50 pg/ml), but periodic slow-tonic contractions (STC: 0.1–0.2/min) in rat-aorta/human renal&uterine arteries. BP-observations: Transformation of depressor response to acetylcholine&electrical-central-vagal stimulation (CVS:55Hz,2ms,5 s,5 V) into biphasic depressor-pressor=dR/pR by nicotine & mercptoethylguanidine (MEG: inhibitor of NO-synthase), also pR-potentiation from VP (5–100 mIU), non-/AHR-600/McN-A-343 & nicotine-like/DMPP: 0.1 μg–100 mg/kg ganglion-stimulating agents, inverting serotoninergic dR. OPEN QUESTIONS 1. Existing of correlation between STC and low-frequency fluctuations (Mayer-waves) & pericytes? 2. Appearance of SPC/STC in human vascular prep. from patients/surgical tissue with hypertonia genuina et renalis, atherosclerosis? 3. Importance of phenomena A&BP for angio-cardiac/cerebral spasms: infarct & apoplexy?
Conclusion: Drugs, endogenic substances & psychosomatic factors could sensitize BP regulatory central, spinal, neural & peripheral structures causing idiopathic hypertension, leading probably to angiocardiac cerebral spasms via biphasic dR/pR or augmented pR by endogenic or exogenic factors. Further observations could help for new therapies in context of UNO-Agenda21 for better health, education, etc. on global level.

E-PS-04 Cytopathology

E-PS-04-001

Metastasis of colon cancer to the thyroid gland: A case diagnosed on fine-needle aspirate by a combined cytological, and immunocytochemical approach

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Objective: Metastasis of colon cancer to the thyroid gland is extremely rare in routine clinical practice. Therefore, it is often not included in the differential diagnosis of patients presenting with malignant thyroid cytology. We report a case of primary colon carcinoma metastasis to the thyroid with cytological features.
Method: This rare case is re-evulated on the basis of the literature
Results: 66-years-old female patient has presented with 1.5 cm firm, solid nodule in the left thyroid lobe. FNA was performed and cell block was prepared by the plasma-thrombin clot technique. Three years ago, she underwent a sigmoid colectomy for adenocarcinoma. On both Giemza and Papanicolau stained smears, abundant cell necrosis was evident; besides necrosis, epithelial cell population showed cells with irregular contours, nuclei were elongated, "cigarlike" shaped, with coarse granular chromatin, which had not reminded primary thyroid carcinoma. Cell block showed that similar morphological features. The cell groups revealed architectural abnormalities with a high degree of cell overlapping; and cribriform arrengement. At higher magnification, cellular atypia was evident; cytoplasms Tumour cells were positive for CK20, CDX2, and negative for TTF-1 and CK7. The case was reported as colon adenocarcinoma metastasis
Conclusion: We were presented this case to kept in mind metastases when examining thyroid FNA

E-PS-04-003

The heat induced antigen retrieval has influence on immunocytochemistry results in alcohol-fixed cell samples

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Objective: Immunohistochemistry (IHC) and immunocytochemistry (ICC) play irreplaceable role in diagnostic. It is well known that antigen retrieval technique has beneficial outcomes on IHC results on formalin-fixed, parafin-embeded tissue samples. The main purpose of antigen retrieval is breaking protein crosslinks which are formed during formalin fixation. It also provides additional advantages, such as use of higher antibody dilution and increase the staining specificity. On the other hand, cytological samples are fixed in alcohol-based fixatives which does not leads to formation of crosslinks thus antigen retrieval technique does not seem to be necessary step in ICC.
Method: Alcohol-fixed HEK293 cell line and patient cytological samples from thyroid gland obtained by fine needle aspiration (FNA) technique were used in this study. We compared indirect two-step ICC staining results performed according to protocol with or without heat induced antigen retrieval for several antibodies.

Results: In most cases, using antigen retrieval allows us to used more diluted antibodies. Staining specificity seems to be also improved.
Conclusion: Using heat induced antigen retrieval technique could improve ICC staining results for diagnostics.

E-PS-04-004
Multinucleated giant cells significance in cervico-vaginal smears
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Objective: Multinucleated giant cells (MGC) in cervico-vaginal smears (CVS) are a part of a wide clinical spectrum varying from physiologic to neoplastic situations. They can be of exocervical, endocervical or inflammatory origin.
Method: We report a case series of 11 conventional CVS showing MGC and analysed at Pathology department of Mongi Slim's Hospital. Clinical informations included the age of patients, their hormonal status and the contraceptive method if used.
Results: Mean age was 45 years old (23–65). All the smears were adequate for evaluation. An accurate diagnosis was made in 7 cases. MGS were encountered in physiologic situations like postmenopausal atrophic smears ($n = 2$) and during gestation with an inflammatory background ($n = 1$). Herpetic cells showing multinucleation and ground-glass appearance were displayed in 2 cases. Atypical squamous cells of undetermined origin (ASC-US) displayed MGC among the other criteria ($n = 2$).
Conclusion: MGC are often encountered in physiologic situations. They can be a part of reactive cell changes seen in inflammatory conditions such as tuberculosis, actinomycosis and herpes simplex infection or associated with radiation. ASC-US, low-grade squamous intraepithelial lesion, glassy cell carcinoma and sarcomas may display MGC. Interpretation can be challenging for cytologists without clinical information but other cytological features can help to make an accurate diagnosis.

E-PS-04-005
Metastatic melanoma in the parotid gland: Diagnosed with fine-needle aspiration
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Objective: Malignant melanoma is relatively uncommon tumour with representation %0.07 of all malignant neoplasms within the parotid gland. Metastatic melanoma in the parotid gland usually arises from head and neck region. The purpose of this report is to describe a rare case of metastatic malignant melanoma in the parotid gland.
Method: Fine-needle aspiration (FNA) is a safe, rapid and easy method to diagnose the parotid gland lesions. The data about the metastatic melanoma in the parotid gland is limited in the literature. A 44-year-old male presented at our hospital with history of a painless mass which rapidly increased in size in parotid gland. The ultrasonographic examination revealed a well defined, approximately 21x13 mm hypoechogenic solid mass that suggested a pleomorphic adenoma as a first possible diagnosis. FNA was performed for the lesion.
Results: Cytological findings were evaluated as 'malignant cytology'.We found that the patient was diagnosed as malignant melanoma in head region 2 years ago from the records. The immunohistochemical markers (HBM-45, Melan A, S100, PanCK, CD45) supported our diagnosis. With all of this findings, metastatic melanoma in the parotid gland was diagnosed.
Conclusion: It should be kept in mind that malign melanoma can rarely make metastasis to parotid gland. Key words: Parotid gland, FNA, Malignant melanoma.

E-PS-04-007
Follow-up of the thyroid fine needle aspiration cytology: An institutional experience
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Objective: To evaluate cytologic- histologic correlation of thyroid fine needle aspiration biopsies.
Method: We retrospectively reviewed thyroid fine needle aspiration cytology results between 2015 and 2016 in our institutional database. Cytological diagnoses were classified as unsatisfactory, benign, atypia of undetermined significance, suspicious for a follicular neoplasm, suspicious for malignancy and malignant. We investigated the malignancy risk for these categories by follow-up histopathology.
Results: Of the 871 cytologies 183 (21 %) were classified as unsatisfactory, 537 (61 %) as benign, 5 (0.57 %) as atypia of undetermined significance, 32 (3.6 %) as suspicious for a follicular neoplasm, 66 (7.57 %) as suspicious for a malignancy and 48 (5.5 %) as malignant. Eighty eight patients underwent surgery, including 25 with benign, 2 with atypia of undetermined significance, 14 with suspicious for a follicular neoplasm, 40 with suspicious for malignancy and 27 with malignant results. Histopathologically confirmed malignancy rates are 32 , 50 , 50 , 80 , 96 % in each category, respectively. Diagnoses on inadequate specimens, sample errors and overlapping cytological features between hyperplastic nodules and follicular adenoma are sources of errors.
Conclusion: Awareness of variable features of follicular lesions, following strict criteria of specimen adequacy, and clinicopathological correlation can markedly reduce false-negative results.

E-PS-04-008
The comparison of the diagnostic utility of manual screening and thinprep imaging system in liquid-based servical cytology
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Objective: This study compares the results of manual screening with the results of ThınPrep automatic method in liquid-based cytology.
Method: A total of 1.500 randomized ThinPrep Pap test That screened manually and archived in 2015 were double-blind reviewed by manual method (MM) and ThinPrep automatic method (TPO). Automatic method was designed only for '22 fields of view'.
Results: The median age of the cases was 40 ± 11,47 years. 'Unsatisfactory for evaluation' ratio was %0.3 for both of the methods. There was a %83.3 increase in the detection of ASCUS with the TPO compared to MM but according to reference results accuracy were higher for TPO than MM. We also noted a %33.3 increase in the rate of LSIL and %20 increase in HSIL by TPO. ASC/SIL ratio was <2 for both of the methods (for MM: %0.9 and for TPO: %1.2). Concordance was best for TPO and reference cytologic diagnoses ($p < 0.05$ and kappa value = 0.631). Sensitivity ratio was higher for TPO and spescifity ratio was similar for both of the methods. We determined a %30 gain on screening time per smear by TPO. But rejection of many samples by yhe system especially because of air bubbles was the limitation of TPO.
Conclusion: Consequently screening only 22 fields of view by TPO also has advantages to manual screening as well as disadvantages like limiting features and high false positive ratio. We are of the opinion that the screening 22 fields of view by TPO must be supported by manual method to decrease the false positive ratio

E-PS-04-009

The value of immunocytochemistry for diagnosing of disputed pleural or abdominal exudates

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Objective: The aim of our study was to evaluate the informative power of the immunocytochemistry of effusion in cases that are difficult to diagnose at the light microscopy
Method: Study was done by using cell blocks in 64 patients with pleural or abdominal effusion. Immunocytochemistry was performed with the usage of a panel of 10 commercially available antibodies in all cases as described elsewhere.
Results: In 26 cases (40.6 %), the immunocytochemistry was performed to determine the nature of the process (benign vs malignant). In 20 cases (31.3 %) study was done to clarify the histogenesis of the tumour; in 18 cases (28.1 %) it was done to determine the organogenesis of the tumour. The efficacy of the cytological study, supplemented by immunocytochemistry, in determining the nature of the process was 88.5 ± 6.4 % (23 of 26 cases), tumour histogenesis – 90.0 ± 6.9 % (18 of 20 cases), organo-genesis – 83.3 ± 9.0 % (15 of 18 cases).
Conclusion: In controversial exudates, the informative value of the immunocytochemical method is 87.5 ± 4.1 %. Immunocytochemistry is the useful method that allows us to clarify cellular elements in the exudate from serous cavities and thereby increase the reliability of the diagnosis.

E-PS-04-010

Non-gynaecological malignancies in Pap Smears

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Objective: Presence of atypical cells in Pap Smears represents a variety of malignant lesions. The scope of this case report is to reveal which types of non-gynaecological malignancies can be involved in observation of atypical cells in Pap Smears.
Method: 7 cases with abnormal cytology originating from non-gynecological malignancies between May 2011 and April 2017 were analyzed retrospectively for determine architectural and nuclear features of tumour cells in Pap smear.
Results: Atypical cells originating from colon (3), rectum (2), pancreas (1) and breast (1) were detected in Pap Smears. These cells showed various cytoplasmic and nuclear features. They predominantly looked like atypical glandular cells with crowded clusters, high N/C ratio, hyperchromasia and loss of polarity. However, in some cases the nature of atypical cells could not be specified because of their resemblance to both atypical glandular and squamous cells. The background was clean in most of them.
Conclusion: Atypical cells in Pap Smears can be a indication not only for uterine and cervical neoplasia but also for non-gynaecological malignancies.

E-PS-04-011

Does the presence of E-Cadherin staining preclude a lobular breast lesion?

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Objective: Technicians: Athanasia Staikou, Athanasia Dinou, Aspasia Kerasiotou E-Cadherin is widely used as an adjunct antibody for differentiating ductal from lobular in situ and invasive tumours. Loss of E-Cadherin expression has been associated with metastases and unfavorable prognosis. The aim of the study was to investigate the pitfalls in the interpretation of E-Cadherin , due to aberrant expressions.
Method: The study comprised 56 breast cancer cases. Papanicolaou stained FNAs and haematoxylin-eosin stained sections were reviewed by the authors. The expression of E-Cadherin in FNAs and sections was evaluated.
Results: 31/39 DBCs showed moderate to strong membrane expression , 6 fragmented membrane staining and 1 complete absence (large tumour with triple negative phenotype) Loss of E-Cadherin was noted in 12/14 LBCs, 1 showed cytoplasmic perinuclear staining of reduced intensity,1 partial fragmented membrane stainining. CIS 3 (2 ductal, 1 lobular), 1 DCIS revealed strong membrane expression and 1 patsy incomplete membrane staining. LCIS demonstrated complete loss of staining. Aberrant E-Cadherin expression was noted in 3/41 (7,31 %) DBCs (2 invasive, 1 DCIS). Aberrant E-Cadherin immunostaining occurred in 2/14 (14,2 %) LBCs.
Conclusion: E-Cadherin is a useful and widely used marker , however attention should be paid to the various patterns of aberrant expression in order to avoid the risk of miscategorization.

E-PS-04-013

Raman spectroscopy as an adjunct to pleural effusion cytology: A preliminary study

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Objective: Conventional cytology is easy to perform and relatively non-invasive. However, there are a certain number of indeterminate cases even though the specimens are examined by experts of cytology. Application of Raman spectrometry (RS) to cytology as an adjunct to morphology is expected to solve such a problem. It has been reported that RS could be applied to cervical and urine cytology, but to our knowledge, application of RS to pleural effusion cytology has not been reported. In this study, we measured Raman spectra of pleural effusion cells and tried to classify them into normal or cancer cells utilizing principal component analysis (PCA) and linear discriminant analysis (LDA).
Method: Raman measurements were performed employing a confocal microspectrometer equipped with 532 nm laser excitation device. Pleural effusion cells were collected from a lung cancer patient and a non-cancer patient. Cytological diagnoses were made by a cytotechnologist (IAC) and a board-certified pathologist. Obviously cancerous cells and mesothelial cells without staining were submitted for the measurements. RS data were analyzed by PCA and LDA. The background spectrum was subtracted from the raw spectrum, and the intensity was normalized at 1086 cm-1.
Results: The spectra obtained from the malignant and benign cells did not seem to be visually different from each other. However, the adenocarcinoma cells were clearly differentiated from the mesothelial cells by 3D-PCA.
Conclusion: The present result suggests the Raman spectrometry with PCA might contribute to accurate cytological diagnosis of pleural effusions in clinical settings, although we need to measure more samples and to eliminate fluorescence from staining reagents.

E-PS-04-014

Cytologic diagnosis of primary breast lymphoma

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Objective: Breast lymphomas are uncommon , represents less than 1 % of all malignant breast tumours and accounts for only 1–2 % of extranodal lymphomas. Breast lymphomas can represent as primary lesions or can be

secondary to a disseminated lymphoma. A primary breast lymphoma diagnosis should be given after excluding secondary involvement. Almost all of the primary breast lymphomas are Non-Hodgkin Lymphoma. Diffuse large B cell lymphoma is the most common subtype.
Method: A 23 year-old female patient presented with a breast mass of 2 months duration. Patient's physical and radiological examination didn't reveal any lymphadenopathy. Hematologic examination results were within normal limits.
Results: Aspirate from the mass included clusters of atypical lymphoid cells exhibiting narrow cytoplasm,large nuclei and small nucleoli with numerous mitotic figures. On immunochemistry study of cell block, these cells showed positivity for LCA, CD 20 , BCL2 and negativity for CK 7. We diagnosed the patient as "Non-Hodgkin lymphoma, B cell type ".
Conclusion: Cytological diagnosis of primary breast lymphoma has significance as the management of the patient change.

E-PS-04-015
Pancreatic mx diagnosis of Clear Renal Cell Carcinoma (CRCC) by fnab- eus-guided: Review of 2 cases
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Objective: The pancreatic MX of CRCC is little frequent (1–2.8 %), since it usually occurs as single pancreatic nodule, with an interval between the resection of the primary tumour and the MX that can be very long (up to 30 years). Conservative surgical resection is the treatment of choice.
Method: Case 1: 82-year-old male diagnosed in April 2016 from CRCC (grade IV of Fuhrman) pT3a. Case 2: 55-year-old woman diagnosed in 1999 by CRCC invading adipose tissue and venous vessels hilar with lymph node relapse in 2000.
Results: Endoscopic Ultrasound (EUS)-EUs-guided Fna, obtaining material for extended cytologic and citobloque which are techniques of SWI. In both cases obtained atypical cells are positive for CD-10; Vimentin and Renal CC, which confirms the Presurgical diagnosis of Metastasis of renal clear Cell Carcinoma.
Conclusion: Before a solid, well defined patient diagnosed of CRCC injury should be suspected MX although the disease-free period is very long. The realization of citobloque with the material obtained by Fna (EUS) is high-value diagnostic. Techniques of SWI for the preoperative diagnosis of the lesion and select patients with CRCC MX for the conservative surgical resection, it improves survival and quality of life of the patient.

E-PS-05 Dermatopathology

E-PS-05-001
A diagnostic challenge in the conundrum of basal cell carcinoma with trichoblastic-like differentiation versus trichoblastic carcinosarcoma
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Objective: The case of a 58-year-old male patient presenting with a right preauricular mass and the difficulty the histopathological aspects of this type of case represents
Method: Grossing of the tissue with histological slides preparation using hematoxylin and eosin and immunohistochemical stains
Results: Histological sections revealed a poorly circumscribed, infiltrative neoplasm composed of epithelial cells arranged in lobules with peripheral palisading and focal retraction of the stroma, numerous and focal keratotic areas with adnexal differentiation. The proliferating mass showed vascular and nerve tropism. Immunohistochemically the epithelial component of the tumour was weakly to moderately positive for Ber-EP4, moderately to intensely positive for AE1/AE3 and negative for Vimentin and EMA, while the sarcomatoid component was negative for Ber-EP4 and AE1/AE3, and positive for Vimentin. At the periphery of the proliferating mass, there were aspects that resembled follicular stroma with CK20 focal positivity.
Conclusion: Consulting the literature and weigh in the histological and immunohistochemical findings a diagnosis of trichoblastic carcinosarcoma is proposed

E-PS-05-002
Analysis of nasal skin biopsies: A 354-case series
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Objective: The aim of this study was to review the main lesion types of the nasal skin and to present a comprehensive list of the diseases that affect the skin that can involve the nose.Incisional/ excisional biopsy with histopathological study is a must in all types of small masses in nose.
Method: A study of 354 patients was done,specimen collected and subjected to histopathological study.These masses were further classified as nonneoplastic (inflammatory, cysts..),benign,premalignant and malignant lesions and the frequency of their occurrence in Kırsehir region,their age and sex distribution were observed.
Results: In general,benign neoplasms were the most common in all lesions(65.2 %,*n* = 231) followed by malignant neoplasms(20.1 %,*n* = 71),non neoplastic lesions(9.6 %,*n* = 34) and premalignant neoplasms (5.1 %,*n* = 18).Nevus(175),basal cell carcinoma(67) and chronic non-specific inflammations(21) were commonest lesions.In malignant neoplasms basal cell carcinoma(67) was more common than squamous cell carcinoma(4);in benign neoplasms,nevus(175),vascular tumours(13) and verruca vulgaris(11) were mostly diagnosed.In premalignant lesions,actinic keratosis(11) and keratoacanthoma(7) were found in 18 patients.Females(226) were more affected than males(128).There were 20 cases under 18 year old.Adolescents/children didn't affected for premalignant and malignant neoplasms.
Conclusion: Any disease that affects the face and nose,mostly depends on ultraviolet exposure.As a result of heterogeneity of skin lesions of the nose,proper education of clinicians and excision biopsy with histopathological study are compulsory.

E-PS-05-003
Gigantic extraocular sebaceous carcinoma: A case report
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Objective: Sebaceous carcinomas are malignant adnexal skin tumours expressing sebocytic differentiation. According to the site of involvement, these neoplasms are classified as ocular or extraocular, with no biological differences, ocular location being more frequent.
Method: We report a case of a 66-year-old woman with a history of breast carcinoma, NST, presenting with a gigantic, exophytic, ulcerated, epicranial tumour mass, measuring 110/74/40 mm.
Results: On gross examination, the tumour appeared sessile, whitish, having an irregular, ulcerated surface, with a hematic crust. The cut section revealed areas of hemorrhage and necrosis. The mass was totally

excised, being surrounded by apparently normal skin. Microscopically, we identified a subepidermal proliferation, with lobular arrangement, consisting of highly pleomorphic epihelioid cells, with brisk mitotic activity, many of the mitotic figures being atypical. Sparse sebaceous differentiation was noticed as multivesicular and vacuolated clear cytoplasm and also scuamous metaplasia as dyskeratotic cells and small keratin pearls. Areas of necrosis with "comedo" pattern centered the large tumour lobules. Immunohistochemical study revealed strong, diffuse positivity for cytokeratins. CEA was negative.
Conclusion: The histopathological aspects and the immunoreactivity were compatible with the diagnosis of poorly differentiated sebaceous carcinoma. Further investigations were recommended for excluding Muir-Torre Syndrome.

E-PS-05-004
Invasive squamous cell carcinoma developed on actinic keratosis, is there a progressive line of carcinogenesis?
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Objective: To verify if evolution towards invasive squamous cell carcinoma (iSCC) in actinic keratosis (AK) is linear – KIN1 to KIN 2 to KIN3 to iSCC
Method: We retrospectively 55 consecutive cases of iSCC developed on AK, correlating the degree of dysplasia with the presence of invasive lesions and tumour grading
Results: Just 20 cases of iSCC had associated KIN3 while 35 cases had KIN2 and KIN1. Most iSCC were well differentiated (30 cases), 19 of them being developed on KIN1 and 2, while we had only 2 cases of G3 iSCC, both developed on KIN3.
Conclusion: Most cases of iSCC are developed on low- and intermediate-grade lesions of KIN, sustaining the hypothesis that progression towards invasive malignancy is not linear. Probably, the first step is field cancerization, numerous cell acquiring mutations leading to KIN. Continuous UV trauma is affecting one cell from the already mutated ones, regardless of grade of dysplasia already obtained, and this additional DNA-lesion triggers the invasive behavior. It is probable that G3 iSCC are more prone to develop on high grade KIN.

E-PS-05-005
Rhabdomyoblastatic transdifferentiation in metastatic melanoma
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Objective: Metastatic melanoma with rhabdomyoblastic differentiation is an extremely rare condition with poor prognosis
Method: A 57-year-old woman was admitted at the Emergency University Hospital in Bucharest due to abdominal pain and upper gastrointestinal bleeding. An CT scan with IV contrast suggested a tumour with considerable enhancement, located in the endopelvic portion of the ileum. At this point, the patient underwent a surgical intervention with removal of the tumour mass. The patient deceased 4 days after the operation due to cardiovascular comorbidities.
Results: On gross examination, the tumour resembled a GIST that was well circumscribed, the cut surface was tan-gray with areas of infarction, hemorrhage and necrosis. Microscopic examination was surprising and revealed two main types of cells: some suggestive for melanoma and others with rhabdoid features. At this point, searching through patient's medical history revealed that she had multiple records of metastatic melanoma. Immunohistochemical tests showed intense positivity for melanocytic markers and rhabdoid markers. CD 117 and DOG 1 were negative, excluding a GIST. Interestingly, Ki-67 expression was lower in rabdhoid cells, as well as HMB-45 expression. The final histopathological diagnosis was intestinal metastatic melanoma with rhabdomyoblastic transdifferentiation
Conclusion: Although rhabdoid features in melanoma have been described and are not uncommon in metastatic disease, true rhabdomyoblastic transdifferentiaton is extremely rare and can be a real challenge even for an experienced pathologist

E-PS-05-007
Pilomatrical carcinoma in the thigh: A case report and review of literature
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Objective: A 51-year-old male patient presented to the outpatient clinic with a history of slowly growing subcutaneous mass in the middle inner aspect of left thigh for 8 months, recently the mass rapidly enlarged.
Method: Microscopic examination of the resected mass showed poorly circumscribed nodular lesion in the deep dermis composed of irregular nests of large pleomorphic basaloid cells undergoing abrupt trichilemmal type keratinization enclosing structurless eosinophilic cells (shadow or ghost cells), focal calcification, and exuberant foreign body reaction with multinucleated giant cells were seen. Focal areas showed infiltrating sheets of tumour cells, with numerous mitoses including atypical forms. Areas of transition into atypical squamous epithelial cells and abundant necrosis were also seen.There was no infiltration of deep resection margin.
Results: The presence of infiltrative nests, pleomorphism, atypical mitoses, and abundant necrosis were leading to a diagnosis of pilomatrical carcinoma, despite the lack of vascular invasion or perineural involvement. A second opinion was taken by two expert dermatopathologists to confirm the diagnosis.The patient was followed up and he did not show any evidence of local recurrence or metastasis for 15 months after the surgery without adjuvant chemotherapy or radiotherapy
Conclusion: The pilomatrical carcinoma is an extremely rare malignant tumour of skin appendages. The diagnosis is often not straight forward and missed due to shared features with its more common benign counterpart. In patients with recurrence or fast growth of pilomatricoma, the diagnosis of carcinoma should be considered. Wide excision with 1–2 cm safety margin is the treatment of choice with regular follow-up to detect recurrence.

E-PS-05-008
CD3+ and CD8+ T-cells in invasive and in situ squamous cell carcinoma (SCC) of the skin and actinic keratosis
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Objective: T-lymphocytes (CD3+) participate in tumour surveillance and their subpopulations either facilitate (regulatory T-cells) or impede (CD8+ T-lymphocytes) tumour growth. The study aimed to examine CD3+ and CD8+ T-lymphocytes in invasive squamous cell carcinoma (SCC) of the skin and adjacent in situ squamous cell carcinoma (ISSCC), actinic keratosis (AK) and normal skin (NS).
Method: Paraffin tissue sections from 124 cases of INSCC, with adjacent ISSCC, AK or normal skin (NS), present in 51, 122 and 122 cases, respectively, were immunostained for CD3 and CD8. The lymphoid infiltrates were evaluated using the Klintrup-Makinen grading scheme. Statistical analysis was performed using

Marginal Homogeneity test. p-values <0.05 were considered statistically significant.
Results: CD3+ and CD8+ T-cells were more numerous in INSCC, ISSCC and AK compared to NS ($p < 0{,}001$ for all comparisons), and in INSCC and ISSCC compared to AK ($p < 0{,}001$, for all comparisons, except for CD8+ T-cells in the ISSCC/AK comparison, where $p = 0{,}002$).
Conclusion: CD3+ and CD8+ T-cell infiltration of the skin increases from NS to AK, and IS/ SCC. Further studies assessing the functional status of the CD8+ infiltrate may provide information with therapeutic implications for immune checkpoint inhibition.

E-PS-05-009
Primary mucinous carcinoma of the skin: A case report with diagnostic considerations
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Objective: To report a case of Primary mucinous carcinoma of the skin (PMCS) - an uncommon tumour of sweat gland origin.
Method: The primary lesion - a right occipital skin nodule from a 70-year-old female was excised and assessed histologically and immunohistochemically. This followed by resection of enlarged regional lymph nodes, which were assessed histologically.
Results: Histology showed the 3.0 cm primary lesion to be a mucin-producing adenocarcinoma with dermal and subcutaneous tissue involvement. Immunohistochemistry was positive for: oestrogen and progesterone receptors, pancytokeratin (CK AE1/AE3), cytokeratin 7 (CK7), carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), synaptophysin, gross cystic disease fluid protein-15 (GCDFP-15) but negative for: cytokeratin 20 (CK20), Her-2/neu, chromogranin A, CD56, thyroid transcription factor-1 (TTF-1), mammaglobin. In situ component with a rim of myoepithelial cells was confirmed by cytokeratin 5/6 (CK5/6) and p63 stains. A diagnosis of PMCS was favoured. Subsequent lymphadenectomy specimen showed metastatic tumour with identical appearances. Clinical workup showed no other primary malignancies.
Conclusion: The diagnosis of PMCS requires exclusion of metastatic mucinous adenocarcinomas from other sites, especially breast. Clinicopathologic correlation is essential. Immunohistochemical confirmation of in situ component with myoepithelial layer, favours dermal origin. PMCS may recur and metastasise, thus, the follow-up and wide excision is recommended.

E-PS-05-010
Case report: An 82-year old woman with an aggressive diffuse large B-cell lymphoma, leg type
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Objective: Diffuse large B-cell lymphoma, leg type is a rare cutaneous lymphoma, characterized by the presence of nodules or tumours on the legs of elderly people, mainly females. We present the case of an 82 year-old woman with a painful, rapidly growing hyperpigmented leg nodule, admitted to the plastic surgery department.
Method: The resected nodule was fixed with formalin 10 %, paraffin embedded, and analyzed using HE staining and immunohistochemical tests.
Results: At gross examination, it was identified a nodular lesion of 4.6/3.5/3.2 cm, uneven colored white areas alternating with and hyperpigmented areas. Microscopy revealed in dermis and hypodermis a diffuse lymphoid proliferation with medium to large sized lymphoid cells with centroblastic or immunoblastic apparence, uneven nuclei, frequently nucleolated and reduced citoplasma. The suprajacent epidermis was atrophic with no epidermotropism. On immunohistochemistry, the tumour cells were diffuse and intense positive for CD20, BCL-2 and BCL-6, and negative for CD10, CD138, CK AE1/AE3 and S100, all consistent with a diagnosis of diffuse large B-cell lymphoma, leg type.
Conclusion: Diffuse large B-cell lymphoma, leg type is a rare entity which should be differentiated from other cutaneous tumours. The survival rate in BCL-2 positive patients is reduced because of frequent relapses, extracutaneous dissemination and poor response to treatment.

E-PS-05-011
Merkel cell carcinoma: A clinicopathological study of 3 cases
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Objective: Merkel cell carcinoma (MCC) is a quite rare aggressive cutaneous neuroendocrine malignancy; first described by Toker in 1972. It is defined loosely by small case series and reviews. Our objectifve is to determine the epidemiological, etiopathogenesis and clinicopathological characteristics of MCC.
Method: It is a retrospective study of 3 cases of MCC collected from our department over a 6-year-period
Results: There were a 64 year old male; 74 and 83 year old female. They presented a red, indurated skin tumefaction which was located respectively on the knee, on the leg and on the forearm. Clinical examination revealed well defined, painless nodule that measured between 2 and 3.5 cm. Patients underwent a wide local excision. The morphological aspects and the immunohistochemical profile are those of MCC.
Conclusion: Merkel cell carcinoma affects predominantly the white advanced age population with male predilection. It presents mainly on the extremities and head and neck. Multiple factors contribute to the etiology of MCC such as ultraviolet radiation, immunosuppression. But since 2008 Merkel cell polyomavirus was found to be the main etiological agent of this skin cancer. Identification of this tumour virus has led to new opportunities for early diagnosis and targeted treatment of MCC.

E-PS-05-012
Cutaneous chromoblastomycosis: A case report
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Objective: Chromoblastomycosis is one of the chronic fungal infection of skin and subcutaneous tissue. Although it is endemic in certain parts of northern and southern America, there are very few reports of chromoblastomycosis in Turkey in literature. Because of that diagnostic challenges can arise.
Method: Sixty-seven year old male presented with a lesion of 5 years, locally excised, then recurred as pruritic erythematous plaque on his left arm. Biopsies were taken. Leishmaniasis, deep mycosis were considered, but being first two biopsies superficial, findings were nonspecific. Direct mycological examination was inconclusive. Another, deeper biopsy was performed.
Results: Histopathological examination revealed pseudoepitheliomatous epidermal hyperplasia, dermal mixed inflammatory response causing abscess formation, and within this infiltrate, presence of brown, round contoured, thick walled fungal organisms. Fungal culture specimens were positive for organism of Fonsecaea spp.
Conclusion: Among chronic fungal infections seen in Turkey, chromoblastomycosis is very rare. Patients can suffer from persistent lesions without appropriate treatment, as seen in our case.

Our case highlights necessity of differential diagnosis of persistent and chronic infectious conditions by both clinicians and pathologists, and importance of repetitive biopsies and taking fungal infections of such kind into consideration in order to reach definitive diagnosis.

E-PS-05-013

Dermal nerve sheath myxoma

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Objective: Nerve sheath myxoma is a rare benign tumour of the extremities that was long confounded with neurothekeoma, but today they must be completely distinguished from one another. This lesion occurs after the age of 35 years and shows a predeliction for females.
Method: A 56-year-old woman presented with a painless distal tumour on the left ring finger that had been present for 5 years. It consisted of a firm, round nodule.Complete excision was carried.
Results: Cut sections of the tumour showed a homogeneous, pale white-grey texture. Histological examination revealed a myxoid tumour comprising very clearly delineated lobules containing pale fusiform cells with small nuclear inclusions. These cells expressed S100 protein, glial fibrillary acidic protein (GFAP) but no CD34, or epithelial membrane antigen (EMA)
Conclusion: This tumour must be completely excised because of the risk of relapse, It must be distinguished from other myxoid tumours of the fingers, which can sometimes be malignant.

E-PS-05-014

Large cd30-positive cells in benign, atypical lymphoid infiltrates of the skin

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Objective: CD30-positive cells characterize lymphomatoid papulosis and anaplastic large cell lymphoma but can also be found in non-neoplastic skin disorders. Cutaneous infectious, drugs and inflammatory diseases may contain a significant number of CD30-positive cells. Recently, CD30-positive atypical lymphoid cells in common non-neoplastic cutaneous infiltrates rich in neutrophils has been described. The authors present a new case of CD30-positive cells arising in a patient with hidradenitis suppurativa.
Method: We report a case of a 37 year old man diagnosed of perianal hidradenitis suppurativa. The patient recieved surgical treatment and was sent to pathology to study.
Results: The biopsy revealed a dense infiltrate of neutrophils, small lymphocytes and hystiocytes throughout the entire dermis, reaching the subcutaneous fat. On high power we observed focally atypical medium-to-large sized blastoid lymphocytes. These cells showed CD20 and CD30 expression, but negativity for cytotoxic markers and Epstein-Barr virus.
Conclusion: Atypical CD30-positive lymphoid cells are frequently found in common cutaneous non-neoplastic inflammatory cells infiltrates rich in neutrophils and eosinophils. This can cause differential diagnostic problems with CD30-positive lymphoproliferative disorders. Careful histological and phenotypic investigations and correlation with the clinical features are necessary for a proper diagnosis.

E-PS-05-015

Malign proliferating trichilemmal tumour: 2 case reports

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Objective: Malignant proliferating trichilemmal tumour (MPTT) is a rare tumour of external root sheath derivation and invades neighboring tissues accompanied with cytological atypia. Most are erroneously diagnosed squamous cell carcinoma (SCC). Indeed, MPTTs may demonstrate biologically more aggressive behavior than SCC. Herein, we report two cases of MPTT.
Method: First case is a 66-year old man presented with a nodular, well-circumscribed lesion of 22 mm in maximum diameter, located occipital region. The second case refers to a 96-year old woman who had a lump on the scalp with a maximum diameter of 50 mm. Both were excised.
Results: Both lesions consisted of intradermal mass composed of lobules of squamous cells. Peripheral palisading and widespread trichilemmal keratinization were seen. Tumoural cells demonstrated moderate degree of pleomorphism, hyperchromasia with focally infiltrative growth and extension into deep subcutaneous adipose tissue. Necrosis was seen and mitoses were numerous in both cases.
Conclusion: SCC and benign proliferating trichilemmal tumour should be considered in the differential diagnosis of MPTT. Trichilemmal keratinization and absence of a premalignant epidermal lesion are important indicators for the diagnosis of MPTT instead of SCC. Regular, non-infiltrative border and absence of cytological atypia distinguish benign PTT from MPTT.

E-PS-05-017

Dermatofibrosarcoma Protuberans of the face: An uncommon presentation

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Objective: Dermatofibrosarcoma Protuberans (DFSP) is a soft tissue tumour appearing usually in young to middle-aged patients, with a slight male predominance, involving more often the trunk (50 %), while head and neck is the less affected site, in 10–15 % of DFSP cases and just 1 % of all head and neck neoplasms. We describe a case of DFSP of the left naso-buccal area in a 60 y.o. woman.
Method: We received a skin segment attached to a subcutaneous nodular lesion 2,5x2,5x2,0 cm in sizes, indicated by the surgeons as "Epidermoid cyst of left naso-buccal area". Multiple sectioning revealed a compact, grayish lesion of elastic consistence
Results: The histological examination of the lesion showed spindled cells with eosinophilic cytoplasm and elongated wavy nucleus, in a fascicular or storiform pattern, that diffusely infiltrate the dermis, subcutaneous fat and underlying skeletal muscles. The immunohistochemical control revealed CD34, Nestin, bcl-2, Vimentin and focally FXIIIa positive cells, while CD68, S100, Actin, FVIII, INI-1, GFAP, CK AE1/AE3 were negative.
Conclusion: DFSP is a low-grade, locally aggressive soft-tissue fibroblastic neoplasm traditionally associated with a high rate of recurrence after surgical excision, uncommonly affecting the face. Its differential diagnosis should include myofibroma, pleomorphic undifferentiated sarcoma, spindle cell melanoma and neurofibroma, all easily distincted by immunohistochemistry.

E-PS-05-018

Vulvar dermatofibrosarcoma protuberans: Report of a case and review of the literature

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Objective: Dermatofibrosarcoma protuberans (DFSP) is a superficial infrequent tumour characterized by high rates of local recurrence and low risk of metastasis. DFSP occurs most commonly on the trunk and proximal extremities and it is extremely rare in the vulva with only a few cases reported.
Method: We present the case of a 82 year old woman with vulvar mass involving the left labium mayor and measuring 8 cm. Six months after surgery the lesion recurred and re-excision was performed.
Results: Microscopically typical features of DFSP were observed both arquitectural(non circumscribed, highly cellular, tight storiform pattern that infiltrates deeply into subcutaneous tissue) and cytologic (monomorphic spindle cells with scant eosinophilic cytoplasm and hyperchromatic nuclei)
Conclusion: DFSP of the vulva is a rare fibrous tumour of low grade malignancy, with a tendency for local recurrence (rates of 20 to 49 % have been reported). However, it rarely metastasizes. Management should be multidisciplinary. Survival rates range from 91 to 100 %. Therefore close follow-up is recommended.

E-PS-05-019
Desmoplastic melanoma: A pitfall for clinicians and pathologists
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Objective: Desmoplastic melanoma is a relatively uncommon variant of spindle-cell melanoma, accounting for less than 4 % of primary cutaneous melanomas. It can arise de novo (90 %) or in association with other melanoma subtypes, most often with lentigo maligna. We report a case of a 74-year-old man who observed change in size in a skin nodule at his back within last 6 months, clinically diagnosed as basal cell carcinoma.
Method: We received a grayish skin nodule measuring 1 cm.
Results: Microscopically a superficial spreading melanoma (SSM) arising in association with a dysplastic nevus, was diagnosed. Breslows' thickness was 2,5 mm without neural involvement. Colliding with the epithelioid dermal component of SSM we observed spindle cells haphazardly within a collagenous stroma showing neurotropism, invading deeper in the reticular dermis. Immunohistochemically, the cells stained positive for S100 and negative for HMB45, Mart1, SMA, PGM1, CD34, FXIIIa, CKAE1/AE3. A diagnosis of desmoplastic melanoma in association with a SMM was made. Breslows' thickness was 4,3 mm
Conclusion: Desmoplastic melanoma can be a diagnostic challenge for clinicians and pathologists alike, because of its non-specific and often banal appearance. Multiple pitfalls exist in achieving the correct diagnosis and evaluation of all melanoma parameters, including the initial clinical diagnosis and interpretation errors under the microscope.

E-PS-05-021
Concomitant sebaceous carcinoma and basocellular carcinoma of the eyelid : A rare case report with review of the literature
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Objective: We present a rare case of concomitant sebaceous carcinoma (SC) and basal cell carcinoma (BCC) in the eyelid and discuss the pathological and ophthalmic features of these tumours.
Method: A 78-year-old man presented with an ulcerated nodular lesion with irregular borders of the right eyelid.
Results: The patient underwent a biopsy followed by a total excision of the lesion. On histological examination, the majority of the tumour was made of a solid pattern of small, round uniform cells with basophilic cytoplasm, partially intermingled with vacuolated cells indicative of sebaceous differentiation with many images of perineural invasion. The cells were immunohistochemically positive for EMA. They were negative for P40, ACE, pS100, HMB45 and Melan A. The periphery of the lesion showed a BCC with the typical nest of basal cells with peripheral palisading. The surgical margins were involved. Based on these findings, the patient was diagnosed with SC and BCC of the eyelid. The case was managed as SC. Close follow-up for possible recurrence or appearance of new lesions was recommended.
Conclusion: SC and BCC can coexist in the eyelid within the same clinical lesion. Because of the potential risk of metastasis of SC, close follow-up of the patients is advisable.

E-PS-06 Electron Microscopy

E-PS-06-001
Comparison of the effect of clomiphene citrate and gonadotropins used for ovulation induction on endometrium: Ultrastructural study
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Objective: Infertility is the inability of the couples to become pregnant in spite of unprotected regular sexual intercourse during a year. Our study aims to examine the histological alterations which could be formed in the uterus tissue as a result of ovulation induction with clomiphene citrate and gonadotropins comparatively at the level of fine structure.
Method: In this experimental study, 36 female 20 weeks old Wistar rats were used. Rats were randomly divided into 6 groups (control, hormone and clomiphene citrate induced, also pregnant group for each drugs) and ovulation induction models have been applied. (n = 6 in each group).
Results: Mild swelling at surface epithelium cells, mitochondrial crystolysis, lipid accumulation was observed at ultrastructural level of hormone induced pregnant group. Basal lamina was thickened. Apical surface specializations were seen to have disappeared in the epithelial cells while the gland structure was quite mature.
Conclusion: In our opinion hormone application affected implantation more in comparing with the clomiphene citrate application but it destroyed the structure at the level of surface and glandular epithelium, and perhaps affected the healthy pregnancy process. On the other hand clomiphene citrate application did not lead to damage throughout tissue.

E-PS-07 Endocrine Pathology

E-PS-07-001
Case report: A woman with unusual presentation of sporadic medullary thyroid carcinoma
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Objective: Sporadic medullary thyroid carcinoma appears as distant metastasis in 15 % of the cases at the time of diagnosis. The most common

sites are the lungs, liver and bone. The broad range of growth patterns and cytologic features make it easy to misdiagnose and start unsuitable treatment. This case report is aimed at raising the consciousness of the fact.
Method: 70- year old lady with hoarseness and lump on a vocal cord and on the neck underwent biopsy of both locations. The biopsy of the vocal cord raised suspicion for carcinoid with unusual location and of the neck revealed cellulae carcinomatosae. The patient was directed to our Institute to start treatment and consultation of the results was ordered.
Results: The morphology and immunoprofile revealed infiltration of mucosa with neuroendocrine tumour with epithelioid-plasmacytoid features, CKAE1/AE3(+), chromogranin(+), calcitonin(+), thyroglobulin(+/-), amyloid(unsatisfactory). Ultrasound showed impalpable thyroid nodule of 1 cm and enlarged lymph node, both confirmed cytologically as medullary carcinoma. Postoperative results: multifocal medullary carcinoma with lymph node metastasis (8/14), staged pT1bN1. One month later cutaneous nodule was excised with diagnose of medullary carcinoma metastasis.
Conclusion: Unusual presentation of medullary carcinoma can prevent or dramatically postpone targeted medical treatment available for advanced disease, as in this case.

E-PS-07-002
Clear cell follicular adenoma of the thyroid: A case report
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Objective: Thyroid tumours with clear-cell features are rare and prone to pose important diagnostic challenges.
Method: We report the case of a 62-years-old female, with no particular clinical history, admitted to the hospital for an asymptomatic, hypoechogenic nodule in the right thyroid lobe, for which right thyroidectomy was performed.
Results: Macroscopical examination revealed a well-circumscribed, 17 mm diameter, whitish thyroid nodule. On light microscopy, the nodule was surrounded by a smooth, thin, connective capsule. The architectural pattern was mostly follicular, but areas of solid growth were also present. The tumour cells were large, with an abundant, watery clear cytoplasm. The nuclei were centrally placed and had smooth contours and no atypia. Immunohistochemistry revealed positive staining for Thyroglobulin and TTF-1, while CD10 was negative. Morphological and immunohistochemical features led to a diagnosis of clear cell follicular adenoma of the thyroid (CCFAT).
Conclusion: CCFAsT should be distinguished from other clear cells thyroid tumours: follicular, papillary and medullary carcinomas (clear cell variant), as well as metastatic renal cell carcinoma and parathyroid tissue. Although rare entities, these tumours might mimic one another and represent a true diagnostic challenge. The patient's history and the tumour's immunohistochemical profile are essential in performing a correct diagnosis.

E-PS-07-003
Mediastinal intrathymic parathyroid carcinoma: Report of a rare case
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Objective: Parathyroid carcinoma is a rare disease accounting for less than 1 % of cases of primary hyperparathyroidism. It can occur in any site in which parathyroid tissue may be found, including mediastinum. We report a rare case of a mediastinal intrathymic parathyroid carcinoma.
Method: The patient, a 43-year-old woman, presented with hyperparathyroidism and hypercalcemia. Parathyroid glands were normal, whereas in MRI a nodular lesion, measuring 3 cm in maximum diameter, was found in the anterior mediastinum. Both tumour and adjacent thymus were surgically excised.
Results: Macroscopically, the tumour was well circumscribed, tan to reddish-brown in colour, with homogeneous soft consistency and foci of cystic change. Histologically, it proved to be an intrathymic parathyroid neoplasm, with focal capsular penetration and minimal invasive growth into adjacent tissues, consistent with parathyroid carcinoma.
Conclusion: Because of the common embryologic origin of the thymus and the inferior parathyroid glands, ectopic parathyroid glands may be found in the anterosuperior mediastinum, adjacent to or within the thymus. Primary mediastinal parathyroid neoplasms are rare, mainly adenomas, whereas carcinomas are extremely rare. Despite their rarity, primary mediastinal parathyroid tumours should be included in the differential diagnosis of anterior mediastinal tumours with or without symptoms of hyperparathyroidism.

E-PS-07-005
Oncocytic adrenocortical neoplasm of uncertain malignant potential: A case report
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Objective: Oncocytic tumours are frequent in thyroid gland, kidneys and salivary gland. They are rarely seen in the adrenal gland and usually nonfunctional and benign. Here, we report a case of oncocytic adrenal tumour of uncertain malignant potential.
Method: An incidental right adrenal mass was found at computerized tomography of a 41-year-old male patient. He was asymptomatic and serum hormonal evaluation showed no abnormality. The patient underwent a right adrenalectomy.
Results: On macroscopic examination, specimen was 10 cm in dimension and weighed 415 grams. Cut section revealed cystic, solid and hemorrhagic areas. Histologic evaluation showed a tumour consists of pleomorphic, large nuclei and large, oncocytic cytoplasm. There were rare mitotic figures without atypical ones. Necrosis was not found but capsular invasion was detected. We reported the case as oncocytic neoplasm of uncertain (borderline) malignant potential.
Conclusion: Weiss system is not available to predict the biological behavior of oncocytic neoplasms. Lin-Weiss-Bisceglia system is more appropriate in these tumours. The presence of one major criteria indicates malignancy and one the minor criteria (large size, necrosis, capsular or sinusoidal invasion) implies uncertain malignant potential. Prognosis of borderline tumours is not predictable. Histological diagnostic criteria should be applied strictly to classify these tumours.

E-PS-07-006
Myelolipoma of the adrenal gland: Clinical and histologic features
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Objective: Adrenal myelolipomas are rare, non-functional, benign tumour-like lesions of the adrenal gland. They are usually found to occur alone in one adrenal gland but not both and there may be a right sided predilection.
Method: We received an adrenal gland measuring 6.5x6x1.4 cm and weighing 32.8gr with its fat and a brown to red tissue fragment measuring 7.5x2.5x2.7 cm and weighing 40.4gr. Histopathological examination was performed.

Results: Microscopic examination from the adrenal's tissue fragment showed partial autolysis details, focal fibrosis, presence of inflammatory infiltrations, macrophages, hemosiderin granules and congested vessels with slightly thickened wall. Macroscopic examinations in both tissue fragments revealed, in an expanded almost universal extent, the presence of mature adipocytes together with extramedullary hematopoietic details. There were also observed haemorrhagic infiltrations, phagocytes, hemosiderin granules and the local presence of amorphous eosinophilic material. All above indicated myelolipoma.
Conclusion: Adrenal myelolipomas can vary widely in size. They are characterized as rare tumours with estimated autopsy prevalence of 0.08 to 0.4 %. They are usually indentified in adults, either incidentally or if complicated by haemorrhage. There is no gender predilection. The tumour affects men and women equally and is most commonly found between the fifth and seventh decades of life with a mean age of 62 years.

E-PS-07-007
Incidental retroperitoneal mass: Ectopic adrenocortical oncocytoma
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Objective: Ectopic adrenocortical adenomas arise from adrenal rests which are seen through embrionic migration line. Until date 35 cases sited different anatomical locations described in the literature. Retroperitoneal location and oncocytic features are extremely rare. We report 56 years old male presented have a mass in retroperitoneal fat tissue on abdomen magnetic resonance imaging (MRI). Adrenocortical neoplasms are the most common tumours of adrenal cortex. Cortical tissue is found either seperately or with medullary tissue in ectopic adrenal rest. It may undergo hyperplasia, adenoma or carcinoma; hence surgical resection is necessary when they were detected.
Method: The surgical spesimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E.
Results: On microscopic examination tumour cells have large eosinophilic granular cytoplasm and small nuclei. They presented nested or solid pattern that surrounded fibrous capsule. There is no mitosis, necrosis, cellular atypia, capsular or vascular invasion. Immunohistochemistry show positive staining with calretinin , synaptophysin , melanA .
Conclusion: Most oncocytic tumours arise from endocrine organs are nonfunctional. No association between tumour and adrenal gland or kidney on MRI suggested that the tumour is ectopic located. Adrenal gland near the tumour capsule and calretinin, synaptophysin, melanA expressions suggested that the tumour originated from adrenal gland.

E-PS-07-008
Adrenocortical carcinoma: A case report
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Objective: Adrenal cortical carcinoma (ACC) is a rare sporadic endocrine malignancy with an incidence of 0.7–2 cases per million population. It most commonly occurs between 40 and 50 years of age, with high morbidity and mortality.
Method: 55-year-old man was previously operated due to left surrenal mass and diagnosis was Cushing Syndrome. After that he applied with nausea and vomiting. Computed tomography scan revealed a 9 cm pelvic mass.
Results: The surgically resected specimen showed a well-circumscribed, partially encapsulated tumour measuring 9.0 cm in greatest dimension. Grossly, the lesion was heterogeneous tan-brown to yellow, hemorrhagic and necrotic. Microscopic examination revealed sheets and nests of high-grade pleomorphic tumour cells with abundant clear to vacuolated cytoplasm with areas of necrosis, a high mitotic index (>10 mitoses/10HPF) Immunohistochemical stains revealed the tumour cells were positive for Melan-A, Vimentin, Inhibin and Synaptophysin, NSE, P53(strongly) and negative for EMA, CK7, CK20. Based upon the morphologic and immunohistochemical profile, the diagnosis was adrenocortical carcinoma.
Conclusion: Adrenocortical carcinoma is a rare but aggressive tumour of the adrenal with an incidence about 1 in a million. It is slightly more common in females. Surgery remains the mainstay treatment for localized disease, but it is often not feasible in more advanced cases.

E-PS-08 Digestive Diseases Pathology - GI

E-PS-08-001
Leiomyosarcoma of lower third of the rectum: Case report of an uncommon neoplasm
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Objective: Leiomyosarcoma of the rectum is a rare entity that comprises less than 0.1 % of all rectal malignancies. Because of its rarity, its diagnosis and treatment often present challenges.
Method: A 46-year-old Caucasian woman with a long history of hemorrhoids that arose after childbirth, turned to a routine examination to the proctologist. During the rectosigmoscopy, a submucosal formation with a diameter of 1 cm was detected. Because of extreme similarity with submucous leiomyoma, a decision was made in favor of a wide excision of the nodule.
Results: Tumour consists of interlacing spindle-shaped cells, with a marked cellular pleomorphism, with large and hyperchromatic nucleus, and abundant eosinophilic cytoplasm. Mitotic figures (16 per 10 HPF) and atypical mitotic figures were also noted. Immunohistochemistry revealed that neoplastic cells expressed desmin, smooth muscle actin, and exhibited negative staining for CD117, CD34, S-100, Cytokeratin pan, Synaptophysin, Chromogranin, HMB-45. Ki-67(MIB-1) was 35 %. Subsequently, a diagnosis of grade II leiomyosarcoma was retained.
Conclusion: Leiomyosarcoma of the rectum is a life-threatening diagnosis that should not be underestimated because of the high risk of local recurrence and hematogenous metastases. Our patient today has 17 months of relapse-free survival. Follow-up monitoring will be conducted.

E-PS-08-002
Recurrent rectal heterotopic gastric mucosa in a child patient
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Objective: To review recurrent rectal heterotopic gastric mucosa in a child patient.
Method: Heterotopia is a condition in which normal tissue is abnormally located in a distinct anatomical site. Heterotopic gastric mucosa (HGM) is rare, having been identified throughout the gastrointestinal tract, more frequently in oesophagus and duodenum, being unusual in the rectum (78 cases reported since 1939, 32 in patients under 16 years old).
Results: Typically, HGM is asymptomatic, nevertheless, when symptomatic, it can present rectal bleeding, stricture formation, or obstruction, being the reason why differential diagnosis with rectal ulcers, gastrointestinal infestations, congenital malformations or inflammatory bowel diseases should be included. The definitive diagnosis of HGM requires

histopathological demonstration of gastric mucosa in rectum, with oxyntic mucosa as the most common histological type. Also, Helicobacter pylori and neuroendocrine cells have been identified in rectal HGM. Malignant degeneration of anorectal lesions has not been reported. The most accepted hypothesis for HGM is explained by the pluripotentiality of stem cells lining the primitive intestinal canal. Although the treatment of choice is resection, usually with optimal results, this patient has relapsed three times.
Conclusion: HGM are infrequent lesions, being even more unlikely those located in rectum. The histopathological diagnosis is accesible.

E-PS-08-003
Retroperitoneal ciliated foregut cyst: A rare malformation
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Objective: Foregut cyst (FC) is an uncommon, benign, solitary cyst consisting of four layers; ciliated pseudostratified columnar epithelium, subepithelial connective tissue, a smooth muscle layer, and an outer fibrous capsule. FCs are classified as bronchogenic, enterogastric or undifferentiated. Friedreich first described the lesion in 1857 and predicted its congenital origin. We present a FC that arised in the retroperitoneum and was difficult to separate from other retroperitoneal cystic mass lesions.
Method: A 27-year-old female presented with flank pain. Abdominal CT revealed a cystic lesion, measuring approximately 7.8 cm in diameter, located near the posterior stomach, superior pole of left kidney and pancreas. Total cystectomy was performed.
Results: Macroscopic examination revealed a 7.8x6 cm unilocular cyst enclosed by a thin capsule, which contained viscous, yellowish fluid. There was no solid component in the lesion. The surgeon confirmed no continuity of the cyst into the surrounding organs. Microscopy demonstrated the cyst to consist of four layers. In focal areas, seromucous glands were seen in the wall. There was no evidence of malignancy. By this findings, this case was diagnosed as retroperitoneal ciliated foregut cyst.
Conclusion: FC located in the abdomen or retroperitoneum is extremely rare and few cases have been described in English literature. Intraabdominal and retroperitoneal locations have been explained by the presence of pleuroperitoneal canals in the early embryonic stage. FC should be considered in the differential diagnosis of retroperitoneal cystic masses includes lymphangiomas, cystic pancreatic tumours, pseudocysts, and hematomas.

E-PS-08-004
Gastrointestinal stromal tumours - histologic staging and prognostic implications
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Objective: Gastrointestinal stromal tumours (GISTs) are mesenchimal tumours derived from interstitial Cajal cells, arising most commonly in stomach (60 %), jejunum and ileum (30 %), and colorectum (5 %). The majority of them are asymptomatic and are diagnosed in patients older than 50 years.
Method: We conducted a retrospective descriptive study of 10 consecutive cases of GIST diagnosed in our department.
Results: There was an equal number of men and women, with a median age of 50 years (range 27–72 years). The main localization was the stomach (40 %), followed by small intestine (30 %), colon (20 %) and anal canal (10 %). Tumours with colonic localisation were the most advanced (T3 and T4 stadialization) and had a higher progression risk. Mitotic index had a median value of 2, the highest index being found in gastric tumours. None of the patients had nodal invasion.
Conclusion: The behavior of GISTs ranges from benign to malignant and, in adult patients, it is predicted by anatomic site, tumour size, and mitotic activity. Altough, according to Miettinen and Lasota, colonic tumours have a good prognosis for a given diameter and mitotic index, these GISTs are usually asymptomatic and are diagnosed in advanced stages.

E-PS-08-005
Morphological and immunohistochemical aspects of premalignant lesions in colonic polyposis. Case reports with short literature review
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Objective: Colonic polyps, either non-neoplastic or neoplastic, are clinicopathological entities of great consequence, because of the subsequent malignancy risk they pose. Thus, the prevention of colorectal cancer, in predisposed patients, is based on the detection and the accurate diagnosis of colonic polyposis, for both solitary, sporadic polypoid lesions and colorectal polyposis syndromes.
Method: In this paper we present a number of colorectal polyps with different morphological and immunohistochemical aspects. The cases were diagnosed in the Clinical Pathology Service of Constanta's Emergency County Hospital.
Results: Colorectal adenoma is currently considered a premalignant lesion, whose incidence evolves parallel with that of colorectal adenocarcinoma. A degree of epithelial dysplasia is always involved in adenomas, making them susceptible to infiltrative and invasive malignant epithelial proliferation, which is why, in certain cases, additional immunohistochemical testing is recommended to establish the correct diagnosis and to choose the appropriate therapeutic management according to the histopathological appearance.
Conclusion: The diagnosis of colorectal premalignant lesions permits choosing the optimal therapeutic management and the proper follow-up for the diagnosed patients, such that colorectal cancer may be prevented.

E-PS-08-006
Osseous metaplasia in an inflammatory caecal polyp: Case report
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Objective: Introduction: Osseous metaplasia has been described in various types of tissues, including neoplastic and non-neoplastic conditions. However, it is an exceedingly rare finding in colonic and rectal polyps, with only twenty-two cases reported to date in the English literature1, 2. We report a case of osseous metaplasia in an inflammatory caecal polyp.
Method: Case report: A 70 year-old male underwent a surveillance colonoscopy and was found to have a caecal polyp which has been excised. Macroscopically, the tan-brown coloured polyp measured 10 mm in diameter, was bisected and submitted for microscopic examination. Histopathologic examination revealed polypoid large bowel mucosa showing a surface cap of ulceration and granulation tissue. There were underlying irregular and dilated colonic crypts within the inflamed stroma. In addition, there was bone formation within the core of the polyp with the spicules of bone separated by loose myxoid stroma [Figure 1]. No dysplasia or malignancy was present. The appearances were interpreted as those of an inflammatory ulcerated polyp with osseous metaplasia.
Results: Conclusion: Occurrence of osseous metaplasia in colonic polyps is quite rare. The exact pathogenesis is still unknown. Theories included

osteogenic stimulation by chronic inflammation, necrosis and calcification as well as transformation of fibroblasts into osteoblasts2.
Conclusion: References: 1. Haynes HR, Wiskin AE, Basude D and Gradhand E. Osseous Metaplasia in a Juvenile Rectal Polyp. J Pediatr Gastroenterol Nutr. 2017 Jan 28. 2. Ebru Zemherİ, Mehtap Toprak, Pınar Engİn Zerk, Seyma Ozkanlİ and Murat Mutus. Inflammatory rectal polyp with osseous metaplasia. Medeniyet Medical Journal 2015; 30(3):143–146.

E-PS-08-007
Xanthomatosis-like regression after chemotherapy: An uncommon phenomenon in a patient with cutaneous metastasis from colon cancer
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Objective: To present an unusual histologic aspect of tumour regression after chemotherapy, in a cutaneous metastasis from colon cancer.
Method: A 68-year-old female was diagnosed with pT3N0 adenocarcinoma of the descending colon for which surgical resection followed by chemotherapy was performed. At 14 months after diagnosis, a nodule was palpated in the periumbilical area, at the level of the incision scar, which was considered a metastatic nodule.
Results: The MRI scan revealed two hepatic metastases. Metastasectomy and cutaneous nodule resection was done. The hepatic metastases were histologically confirmed. The tan-brownish nodule showed under microscope an intact epidermis. In the dermis, diffuse proliferation of histiocytes-like cells was observed. These cells were marked by CD68 and CD44 and showed aberrant cytoplasmic positivity for CDX2. No positivity for keratin AE1/AE3, keratin 20, CEA or S100 was observed. These cells probably occurred as result of disintegration of cutaneous metastatic tumour cells after chemotherapy.
Conclusion: Clusters of foamy histiocytes occurring in the dermis may be considered as a pathological response to chemotherapy, similar to the regressive alteration signs described for the primary gastrointestinal carcinomas. They can occur as result of an epithelial-mesenchymal transition phenomenon induced by chemotherapeutics. This paper was partially supported by the Studium Foundation, projects frame 136/2017.

E-PS-08-008
Clear cell sarcoma-like tumour of the gastrointestinal tract, a rare entity: Our experience with three cases treated in our centre
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Objective: CCSLGT is a rare and aggressive neoplasm. It occurs within gastrointestinal tract frequently with metastatic disease. Affects young adults without any gender prevalence
Method: These were one male and two female aged 41,35 and 36 years old respectively. The two patients in where clinical information was available presented with intestinal wall tumours with numerous regional lymph nodes affectation at the time of the initial diagnosis.
Results: All tumours presented a highly diffuse and infiltrative grown pattern, with focal pseudopapillary arquitecture. Tumours were predominantly round cell with clear cytoplasm and conspicuous nucleoli. Vascular invasion and multinucleated osteoclast-like giant cells were seen. Immunohistochemistry stains were negative for cytokeratin whereas were intensively and diffusely positive for S100 protein and vimentin. Melan A, HMB45, c-KIT, DOG1 and neuroendocrine markers resulted negative. FISH study showed EWSR1 gene rearrangement in all three cases.
Conclusion: CCSLGT presents as a poorly differentiated tumour. The inmunoprofile excludes carcinoma and makes as a main differential diagnosis metastatic melanoma (MM) and clear cell sarcoma (CCSST) CCSLGT does not express neither Melan-A or HMB45 (which are present in MM and CCSST). CCSLGT and soft tissue CCS harbor the rearrangement of EWSR1, feature that does not occur in MM.

E-PS-08-009
The evaluation of appendiceal mucinous neoplasms with a new classification system
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Objective: Appendiceal mucinous neoplasms constitute a diagnostic spectrum ranging from adenoma to mucinous adenocarcinoma. Many classification systems have been proposed until today with the purpose of reflecting the histomorphological diversity of neoplasms in this range and their clinical correspondence, and to form a common terminology between the pathologist and clinicians.
Method: According to the Modified Delphi Consensus Protocol, non-carcinoid epithelial tumours of the appendix were categorized in 8 histomorphological architectural groups. These groups are adenoma, serrated polyp, low grade appendiceal mucinous neoplasm, high grade appendiceal mucinous neoplasm, mucinous adenocarcinoma, poorly differentiated adenocarcinoma with signet ring, signet ring cell carcinoma, and adenocarcinoma. We retrospectively evaluated 19 cases who were diagnosed with appendiceal mucinous tumours. We examined the updated counterparts of the previous diagnoses according to the new classification criteria.
Results: In our re-evaluation, 6 cases were diagnosed as serrated polyp. There were 11 cases in the low grade appendiceal mucinous neoplasm group and 2 cases in the mucinous adenocarcinoma group.
Conclusion: By this review,we provided an updated perspective to the pathological features of the appendiceal mucinous neoplasms. Key words: appendix , mucinous neoplasm, rare tumours.

E-PS-08-010
Prophylactic total gastrectomies in Hereditary Diffuse Gastric Cancer (HDGC): Analysis of 17 cases associated to one novel pathogenic germline CDH1 gene mutation
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Objective: HDGC is an autosomic-dominant hereditary cancer syndrome caused by germinal mutations in the CDH1 gene (codifies for adhesion protein E-cadherin). Lifetime risk of diffuse gastric cancer (DGC) in carriers of CDH1 pathogenic mutations is up to 80 %. Therefore, prophylactic gastrectomy is recommended in these individuals. We present the results of 17 prophylactic gastrectomies from the same family performed between 2013 and 2015.
Method: Genetic testing of CDH1 by Sanger was performed in a family with multiple relatives affected by DGC. Endoscopy and random biopsies were done prior to surgery. Seventeen prophylactic gastrectomies in mutation carriers were performed. Each specimen was wholly sectioned (cassettes median: 203) to look for occult cancer cells.
Results: Genetic testing of CDH1 by Sanger was performed in a family with multiple relatives affected by DGC. Endoscopy and random biopsies were done prior to surgery. Seventeen prophylactic gastrectomies in mutation carriers were performed. Each specimen was wholly sectioned (cassettes median: 203) to look for occult cancer cells.
Conclusion: In the analysis of prophylactic gastrectomies in CDH1-mutation carriers total inclusion of the specimens is essential to detect

cancer cells. E-cadherin is confirmed as a useless screening marker for germline pathogenic variants.

E-PS-08-011

Case report: Mucinous cystic neoplasm of the liver in a young patient

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Objective: Mucinous cystic neoplasm of the liver (MCN-L), previously called hepatobiliary cystadenoma, are rare, and are seen almost exclusively in women.
Method: Twenty-four year-old female presented with abdominal pain,jaundice and swelling.The CT scan that revealed a large cystic formation with internal septas.A radiological diagnosis of hydatid cyst was offered.The patient underwent surgery,and the fully resected cyst was sent for histopathological examination.Macroscopically, a multilocular cystic lesion,13 x 10x2.6 cm,grey-tan color, with hemorrhagic areas were seen.Microscopically, there was a cyst wall lined by biliary type of columnar epithelium with no nuclear or cellular atypia.The epithelial cells had apical mucin.The underlying mesenchymal stroma was a resemblent of the ovarian stroma .The ovarian stroma of tumour was confirmed by Estrogene reseptor, Progesterone Reseptor and CD10 stains, that all were positive.The epithelial cells were positive for MUC-5 AC but not for MUC-1, MUC-2 and MUC-6.
Results: Final diagnosis was MCN-L,and after the surgery levels of liver function tests and CA 19-9 decreased to the normal levels .
Conclusion: The World Health Organization classification defined MCN-Liver as a counterpart of MCN of the pancreas.Ovarian-like stroma is required to establish the diagnosis of MCN-L.MCN-L should be thought when imaging findings suspecting cystic lesions of liver.

E-PS-08-012

Gastric inflammatory myofibroblastic tumour: Case report and review of the literature

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Objective: Inflammatory myofibroblastic tumour (IMT) is a lesion of children and young adults that mainly develops in soft tissues. Whether reactive or neoplastic, its pathogenesis is still poorly understood. Few cases of primary gastric IMT have been described. Clinical presentation and imaging are non-specific, therefore histological examination is mandatory for the diagnosis. We present the case of a primary gastric IMT occurring in an infant with review of the literature.
Method: An 8 months old female infant presented to the emergency after episodes of hematemesis and melena. Clinical examination showed pallor, hypotonia, and tachycardia. Hemoglobin concentration was at 3.1 g/dl. CT Scan revealed a 10 cm exophytic left abdominal mass communicating with the greater gastric curvature. Partial gastrectomy was performed.
Results: Microscopic examination showed a proliferation of spindle cells accompanied by an inflammatory infiltrate of plasma cells, lymphocytes, neutrophils and eosinophils. On immunostainings, the spindle cells were positive for smooth muscle actin (SMA) and anaplastic lymphoma kinase (ALK) and negative for CD117. These features were consistent with IMT.
Conclusion: IMT should be considered in the differential diagnosis of a gastric mass in children. Complete excision of the lesion is curative in most of the cases but the possibility of local recurrence justifies close follow-up.

E-PS-08-013

Brunner's gland hamartoma: Unusual presentation

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Objective: We herein describe a rare case of Brunner's gland adenoma causing gastrointestinal hemorrhage.
Method: A 57 year-old man was diagnosed with duodenal mass during endoscopy, after several hemorrhagic episodes. Endoscopic resection of the tumour was performed.
Results: The resected specimen showed a light brown colored, firm and polypoid mass measuring 2, 5 x 2 x 1 cm. The surface was smooth without any erosions or ulcer. The cut surface was firm, and lobulated. Microscopically, the tumour was covered by small intestinal mucosa and composed of lobules of proliferated Brunner's glands with ducts separated by irregular bands of fibromuscular stroma. Paneth cell change was noted in some of the glands. There was no evidence of dysplasia. According to these findings, a diagnosis of Brunner's gland hamartoma was made.
Conclusion: Brunner's gland hamartoma is a rare benign neoplasm of the duodenum that has a low propensity for malignant transformation. Despite their benign nature, they can cause serious symptoms including life threatening hemorrhage or anemia. In these cases, surgical removal is the treatment of choice.

E-PS-08-014

Autoimmune duodenitis rich in igg4-positive plasma cells

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Objective: Immunoglobulin IgG4-related disease is characterized by serum IgG4 elevation and tissue infiltration by IgG4-positive plasma cells. We present a patient positive for ANA and duodenitis rich in IgG4-positive plasma cells.
Method: A 6-year-old female patient with diarrheal stools (eight per day) during 2 years, fluid, without mucus or blood, vomiting, abdominal distension, and treatment with oral serum and diet. Consultation for persistent diarrhea, hypoxia, asthenia, adynamia, pallor, and weight loss. Normal blood count levels, prolonged coagulation times, hypoalbuminemia, anticardiolipin and positive ANA test.
Results: Endoscopy evidenced erosion and flattening of duodenal villi. Hematoxylin-eosin sections showed erosion in the duodenal mucosa, architecture distortion by villous atrophy, absence goblet cells, and Paneth cells without brush border loss. Lamina propria presented severe lymphoplasmacytic inflammatory infiltrate up to 12 eosinophils (40x), neutrophils permeating the glandular epithelium. No increase in intraepithelial lymphocytes. The IgG4 immunohistochemistry showed the presence of more than 10 IgG4-positive plasma cells (40X). The electron microscopy corroborated a severe atrophy and flattening the villi without brush border loss.
Conclusion: Autoimmune duodenitis rich in IgG4-positive plasma cells is a rare disease, with few published cases. It highlights the importance of complementary studies in these patients for diagnosis of duodenitis with IgG4-positive plasma cells related to systemic autoimmune diseases.

E-PS-08-015

Mucinous carcinoma arising in a tailgut cyst

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Objective: Tailgut cysts (TGC) are considered remnants of the embryological postanal gut. They are usually diagnosed in middle-age women and need to be differentiated from other retrorectal cystic lesions.
Method: A 55-year-old female with proctalgia was investigated and subsequently found having a TGC, revealed on CT-pelvis and rectal MRI

Surgical excision was performed, using trans-sacral excision and the 'Kraske' technique. Results: Microscopy revealed a multilocular cyst, lined

Results: Microscopy revealed a multilocular cyst, lined by columnar epithelium, which showed areas of dysplasia as well as malignant transformation. The neoplasm displayed a tubular pattern with significant production of extracellular mucin and formation of large mucin pools. The neoplastic cells were positive for CK20 and CDX2, while CK7 was positive in a small number of neoplastic cells. Also seen were areas of necrosis and calcification. However, elements derived from other germ layers, such as skin adnexa, neural tissue, heterologous mesenchymal tissue as cartilage and bone, were absent. All the above set the diagnosis of mucinous carcinoma arising in a TGC.

Conclusion: The vast majority of TGCs are benign, however malignancies are reported arising from this entity. there are no established guidelines for management of TGCs harboring adenocarcinoma, but most oncologists suggest adjuvant chemoradiotherapy, due to reported high local and systemic recurrence rates.

E-PS-08-017

Gastrointestinal stromal tumours: About 16 cases

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Objective: To analyze the clinicopathological features, immunohistochemical and molecular profiles of GIST.

Method: This is a retrospective study of 16 GIST collected at the pathology department of the university hospital Mongi Slim over six years from 1st January 2010 to 30th March 2016.

Results: The average age of our patients was 65,18 years (30-78 years) with a female predominance : sex ratio M/F = 0,33.The tumour was found in the stomach in 8 cases, small intestine in 3 cases, duodenum in 2 cases, mesentery in 2 cases and rectum in one case. The mode of revelation was epigastralgia in 5 cases, gastrointestinal bleeding 4 in cases, abdominal pain 3 in cases and peritonitis in one case. In two cases, the tumour was incidentally discovered. The average tumour size was 6,85 cm (1,7 to 16,5 cm). All patients underwent surgical treatment. Histological examination of the surgical specimens revealed a tumour proliferation of spindle cells in 13 cases, epithelioid cells in one case and mixed in two cases. The tumours exhibited in 81% variable intensity labeling for c-kit. The tumour was classified according to the classification of Miettinen and Lasota as very low risk of recurrence in four cases, low risk in 5 cases, moderate risk in two cases and high risk in 5 cases.

Conclusion: GIST is one of the best examples of the interest of current research in oncology. Molecular biology plays an important role in this disease. The current development of new molecules, not only inhibiting C-Kit and PDGFRa but also other relevant targets, will eventually allow a permanent cure.

E-PS-08-018

Primary Hodgkin lymphoma of the stomach - a case report

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Objective: Primary Hodgkin lymphoma of the gastrointestinal tract are extremely rare. They are considered primary if several criteria are meet, namely, the bulk of the disease is located in the stomach, absence of superficial or mediastinal lymphadenopathy, absence of organomegaly or bone marrow involvement and normal result on blood count. We report a case of primary Hodgkin lymphoma of the stomach.

Method: Patient was a 46 year -old male who complained of general fatigue and weight loss. Upper endoscopic revealed an ulcerated lesion with 8,5 cm on the posterior wall of the body of the stomach. Biopsy revealed a lymphoma.

Results: Total gastrectomy with splenectomy and partial pancreatectomy was performed. The tumour bulk was located in the stomach and invaded spleen and pancreas. Regional lymph nodes were involved. Microscopically a lymphoid tumour with Hodgkin and Reed-Stemberg cells (CD15+, CD30 +, CD20 -), accompanied by a rich inflammatory / reactive background was observed. The patient underwent postoperative chemotherapy, and died 3 months after surgery.

Conclusion: Preoperative diagnosis of Hodgkin disease in the stomach is difficult. Only few cases have been correctly diagnosed on biopsy material. As rare, differential diagnosis should be made with other lymphomas.

E-PS-08-019

Intestinal schwannoma: A rare colonic lesion

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Objective: We present a case of colonic schwannoma, a lesion associated with neurofibromatosis type 2 but representing a rare gastrointestinal mesenchymal tumour in its sporadic form.

Method: A 56-year-old female presented with an episode of hematochezia. Colonoscopy revealed a polypoid, intraluminal, 4 cm mass in the sigmoid colon, with a focal surface ulceration, that was removed endoscopically. Microscopically, the tumour consisted of spindle cells in fascicular or vague palisading arrangement, within a loose vascularized stroma. Immunohistochemically, tumour cells exhibited diffuse positivity for S-100, CD34 and focally for CD31, but were negative for DOG-1, CD117, desmin and smooth muscle actin. Mitotic figures were rare to absent. Colonic schwannoma was diagnosed. No additional treatment was administered and no recurrence was observed during the 6-month endoscopic surveillance.

Results: Colonic schwannomas usually manifest as polyps that may ulcerate. Diffuse immunoreactivity for S-100, is of outmost diagnostic value, while reactivity for CD117, CD34, actin or other muscle markers is seen in GISTs or smooth muscle tumours. Treatment options include polypectomy or segmental colectomy with free margins, due to the low risk of recurrence.

Conclusion: Colonic schwannoma is a rare tumour with a benign behavior that should not be confused with GIST or colonic leiomyosarcoma

E-PS-08-020

Giant submucosal lipoma in pyloric region of the stomach: Case report

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Objective: Gastric lipomas are account for less than 1 % of all tumours of the stomach. They are very rarely localized in pyloric region.

Method: We present a female patient aged 61 years, who was admitted to our hospital for surgical treatment of tumour of the stomach.

Results: The patient was endoscopic diagnosed with tumour mass in the pylorus of the stomach. The tumour was described as oval, its wide base was attached to the stomach wall and covered with eroded mucosa. Anamnestically the patient has suffering nausea, vomiting and appearance of blood in the stool for 6 months. In laboratory findings we found anemia. Billroth I gastric resection is done. Macroscopically, we find tumour node in the pyloric area sized 6x5x3 cm, which is movable compared to mucosa and the muscle layer. On rapid frozen sections, tumour of adipose tissue origin is found. On definitive pathohistological samples is diagnosed: Submucosal lipoma. Fifteen months after the surgery, the

patient was with no complaints of gastrointestinal tract and laboratory findings were within normal values.
Conclusion: Submucosal lipomas of the stomach are rarely benign neoplasms, they could imitate the clinical symptoms of malignant tumours. Surgical resection is the method of choice for the treatment of giant lipomas.

E-PS-08-021
Acantholytic squamous cell carcinoma (ASqCC) of the oesophagus: Report of an extremely rare case
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Objective: In Japan, esophageal cancer is usually squamous cell carcinoma (SqCC), except for Barrett's adenocarcinoma. ASqCC is rarely seen in oral or skin cancers. We report an extremely rare case of ASqCC arising from the oesophagus.
Method: We examined ASqCC, clinically, histologically and immunohistochemically.
Results: The patient was 49 year-old Japanese male, who noticed dysphagia in 2012. The tumour was found in the lower oesophagus. The biopsy specimen showed poorly differentiated SqCC with gland-like degeneration. Neoadjuvant chemotherapy was performed, and then subtotal esophagectomy on 2013. Macroscopically, the lower esophagus showed moderate stenosis with epithelialization on the surface. He is alive without disease, 4 years after operation. Histologically, the tumour showed SqCC with gland-like structures in the tumour nests with keratinization, but there was neither evidences of mucin production nor true glandular differentiation, due to the negativity for both mucin stain and CK7, which is a marker for ductal differentiation. This tumour showed the decrease of E-cadherin expression in the tumour nests.
Conclusion: We finally diagnosed that this case was ASqCC of the oesophagus. ASqCC is rarely seen in oral cavity or skin, but its prognosis remains controversial. This case, which is the first one of esophageal ASqCC, indicated good outcome.

E-PS-08-022
Goblet cell carcinoid of the gallbladder: A rare case
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Objective: Neuroendocrine carcinomas arising in gallbladder are very rare.
Method: A 67 year-old female patient has undergone cholesistectomy for her abdominal pain and suspicion of gall bladder stones.
Results: Macroscopically a submucosal 3 cm mass located in the corpus was seen. Microscopically the tumour was composed of small rounded nests of signet ring-like cells.. All of the signet ring-like cells were positive for chromogranin, synaptophysin and CD56. The Ki 67 proliferation index was 80 % and there were 33 mitotic figures per ten hpf. The diagnosis was goblet cell carcinoid.
Conclusion: neuroendocrine carcinomas are very rare in the gall bladder and goblet cell carcinoids are even rarer. It is important differentiate from signet cell carcinoma.Ths tumour has a very poor prognosis and unfortunately the patient is dead.

E-PS-08-023
Malignant transformation of gastric hyperplastic polyp: Case report
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Objective: Gastric hyperplastic polyps (GHP) are detected during 1–6 % of gastrointestinal endoscopies. Only 2–3 % of GHPs, usually the larger ones (> 1–2 cm), show features of focal intraepithelial neoplasia (IEN) or cancer.
Method: We describe the case of focal adenocarcinoma developed in GHP.
Results: A 56-year-old man presented with abdominal pain. Endoscopic study detected large polyp of the antrum, 5,5x4,5x2,5 cm in size, with brown granular surface, lobular structure, pedunculated (Yamada type IV). Endoscopic polypectomy was impossible due to high risk of postoperative complications. Thus laparoscopic antrum resection of the stomach was performed. On histological examination the polyp was identified as GHP with focal high grade IEN of the surface epithelium and two independent focuses of well differentiated tubular adenocarcinoma: 3,5x3 mm and 4x2 mm. No signs of stalk invasion were detected. Immunohistochemical study revealed elevated expression of Claudin-3, Ki67 in cancer glands and nuclear expression of Claudin-3 in dysplastic glands. Strong expression of CDX-2 detected in adenocarcinoma and IEN confirmed intestinal type of differentiation. Expression levels of Claudin-1, Claudin-4 and β-catenin did not differ between adenocarcinoma and GHP-areas.
Conclusion: The polyp was removed radically. There were no signs of progression or relapse 3 month later.

E-PS-08-024
Solitary rectal inflammatory cap polyp: A case report
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Objective: Rectal bleeding combined with the presence of a rectal-mass has been traditionally associated with the presence of malignant disease. Inflammatory-cap-polyp(ICP) is a relatively new and still undefined rare entity which mainly involves the rectosigmoid.
Method: Case Report: A 83-year-old female was admitted to hospital with intermittent rectal bleeding that has lasted for 3 months. Colonoscopy revealed the presence of a 1 cm polyp with fibrinopurulan exudate on its surface in rectum 2nd cm above the dentate-line. Colonoscopic polypectomy was performed.
Results: Histopathological examination showed polypoid tissue exhibiting elongated, dilated/tortuous hyperplastic colonic crypts in its central part and covered in most superficial regions by a "cap" of inflamed and ulcerated granulation tissue, fibrin and inflammatory exudate. The intervening lamina propria contained increased numbers of acute and chronic inflammatory cells. The findings were considered consistent with the diagnosis of ICP.
Conclusion: ICP is a lesion of mostly rectosigmoid colon, clinically miscible with malignancy. Patients often present with diarrhea, mucoid stools, a bleeding polypoid gastrointestinal lesion and/or tenesmus. Most ICPs are small sessile/semipedunculated lesions that range in size from a few milimeters to 2 cm. Differential diagnosis of ICP from malignancy is important for the treatment as the isolated polyps are treated by simple polypectomy.

E-PS-08-025
Myoepithelial hamartoma of the small bowel caused intestinal obstruction: Report of a case
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Objective: We presented here a case of ileal myoepithelial hamartoma (MEH), which is a very uncommon lesion of the small intestine that may represent displaced pancreatic anlage from alongside the gastrointestinal tract or pancreatic metaplasia of endodermal tissues.
Method: Clinical data and histopathology analysis.

Results: The patient was a 47-year-old man who was admitted to the hospital due to intestinal obstruction. Tumour mass 1,6 × 1,1 cm in size was revealed in the wall of the ileum and surgically removed. Histologically, cribriform mucous glands, dilated and nondilated ducts surrounded by the disorderly arrangement of smooth muscles, characterized the well-circumscribed submucosal mass. Epithelial component of tumour was negative for MUC2, stromal component was SMA-positive. The diagnosis of myoepithelial hamartoma was done.
Conclusion: Myoepithelial hamartoma is usually asymptomatic and found incidentally. Meanwhile, it should be kept in mind to avoid misdiagnosis of malignancy and unwanted radical surgery.

E-PS-08-026
Brunner's gland hamartoma
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Objective: Brunner's gland hamartomas are rarely encountered as polypoid nodules in the proximal duodenum. The nomenclature of the Brunner's gland lesions in the literature is not well established. Difference in the meaning of the terms "Brunner's gland hyperplasia" "Brunner's gland hamartoma" and "Brunner's gland adenoma" remains uncertain and will be discussed on our case.
Method: Macroscopically, 6,5x5,5x3,5 cm, yellow-cream colored, lobulated, solid appearing, tumoural mass with microcystic changes was seen on the duodenal resection. Histopathologically, densely packed lobulated hyperplastic Brunner's glands were located on the wall. Fibromuscular septas, smooth muscle fibers and pancreatic ducts were also present inside the lesion. Immunohistochemically, the glands were positive for MUC6, CK19 and CK7 and they showed low proliferative activity.
Results: The final diagnosis was Brunner's gland hamartoma.
Conclusion: Tumours like Brunner's gland hamartomas of the duodenum are rare and difficult to diagnose because of their nonspecific symptoms. Brunner's gland hamartoma should be kept in mind on a duodenal mass.

E-PS-09 Digestive Diseases Pathology - Liver and Pancreas

E-PS-09-001
Evaluation of liver metastases: An 11-year experience
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Objective: The liver is one of the most common metastatic sites of primary carcinomas.
Method: In this study, the records of the biopsies, resections and fine needle aspirations of the liver between 2006 and 2017 were reviewed retrospectively.
Results: The mean age was 60.2 years, with 53 % males and 47 % females. In a total of 528 specimens, there were 272 needle core biopsies (NCB), 153 metastasectomies, 53 wedge resections, 23 segmental resections and 27 fine needle aspirations (FNA). Amongst 437 (82.7 %) cases with metastasis, there were 384 (87.8 %) malignant epitelial tumours, 11 (2.51 %) mesenchymal tumours, 6 (1.37 %) malignant melanomas and 36 (8.23 %) neuroendocrine tumours. Primary neoplasms in the liver were seen in 12 patients. Fifty-two of the cases were negative for tumours because the surgeons could not reach the tumoural area. A history of primary carcinoma was present in 294 patients. The first finding in 7 patients was a mass in the liver and primary carcinoma diagnosis was obtained after the biopsy. In 16 patients despite all the clinical, radiological and pathological investigations the site of primary carcinoma could not be reached while 67 patients without follow-ups were excluded.
Conclusion: The present study demonstrates that, it can be very difficult to find the primaries of some liver metastases.

E-PS-09-002
Ciliated hepatitic foregut cyst in a rectal cancer patient
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Objective: Ciliated hepatic foregut cyst is a rare cystic liver lesion of presumed embryonic origin. Less than 100 cases have been reported in English literature (Bishop et al., 2015). Our aim was to present a case of ciliated hepatic foregut cyst in oncologic patient.
Method: Medical documentation, pathology slides and radiologic investigations were reviewed in the context of up-to-dated scientific literature.
Results: By computed tomography, a 55-year-old male was diagnosed with unspecified lesion in the liver segment IV. The patient suffered from rectal cancer (T4N1M1G2R0) since 2013, thus liver metastasis was suspected. The pathological hepatic focus was resected. Grossing revealed a cystic lesion (1.2x1.2x2cm) with greyish mucinous content. Microscopic examination showed cyst lined by ciliated pseudostratified columnar epithelium with isolated goblet cells. Cellular atypia or mitoses were absent; proliferation fraction was low. Subepithelial connective tissue and isolated bundles of smooth muscle were also found within the cyst wall. Thus, diagnosis of ciliated hepatic foregut cyst was issued.
Conclusion: Due to variable radiographic appearance of ciliated cyst, diagnosis can be difficult necessitating differentiation from wide spectrum of hepatic lesions, mostly—primary or secondary tumour. Here we have demonstrated recently originated ciliated hepatic foregut cyst in patient with rectal cancer history, further complicating diagnostic considerations.

E-PS-09-003
Congenital poorly differentiated cystic adrenal neuroblastoma with liver metastases: Case report
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Objective: The most common site of the Congenital neuroblastoma is suprarenal medulla. Cystic metastasis to the liver is rare. Such cases can be misdiagnosed as another tumour, such a mesenchymal hamartoma, vascular and bile duct abnormalities, and even echinococcal cyst.
Method: Here we present a rare case of 2 months old newborn boy with solid-cystic liver mass, misdiagnosed clinically as a Caroli's disease. Computed tomography revealed large solid-cystic lesion of the liver, and right suprarenal gland. Biopsy was taken from both sites. To reveal the true nature of the tumour, routine histology and immunohistochemistry was done.
Results: Tumour had a small round cell tumour type histologic features - sheets of small round cells forming small lobules and separated by fibrovascular septa. Formation of the Homer Wright rosettes was observed. Tumour was negative for S100, Desmin, Vimentin, CD99, PanCK, GFAP, EMA, aSMA, CD43. In neoplastic cells, strong expression of the neuroendocrine markers was observed (Synaptophysin+. CD56+). Ki67 positive in more than 40 % of cells.
Conclusion: We represent a rare case of neuroblastoma of the right adrenal gland with cystic metastasis of the liver, clinically misdiagnosed as a Caroli's disease. In cases of the liver congenital cystic lesions neuroblastoma should be considered in differential diagnosis.

E-PS-09-004

Eukaryotic initiation factors (eIFs) impact neuroendocrine tumourigenesis

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Objective: Neuroendocrine tumours (NETs) are a heterogeneous group of tumours. One major activity in every cell is translation of mRNA to the corresponding protein, which plays an important role in cancer development. Crucial for translation process are eukaryotic initiation factors (eIFs), which are regulated by the mammalian target of Rapamycin (mTOR)-pathway. Mutations or deregulated expression of eIFs influence cell growth and proliferation, contributing to carcinogenesis. We aimed to investigate the eIFs function in NETs development.
Method: Gastroenteropancreatic NETs (G2) and their corresponding liver metastases from four individuals, as well as 2 different NET cell lines were analyzed on protein expression level for various eIFs and mTOR members by Western Blot compared to non-neoplastic tissue.
Results: eIFs were altered in primary NETs. In contrast, liver metastases displayed fewer alterations in eIF expression. Furthermore, eIFs and members of the mTOR pathway were changed in different NET cell lines pointing to a possible mechanistic link between NETs and mTOR.
Conclusion: Our data suggest a contribution of eIFs and mTOR signaling to the development and progression of NETs. A better understanding of the molecular mechanisms leading to neuroendocrine tumourigenesis is crucial for establishing novel and tailored treatment strategies for NET patients

E-PS-09-005

Adenosquamous carcinoma of the liver: A rare case report

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Objective: Adenosquamous carcinoma (ASC) is a rare tumour of the liver. They account for approximately 2–3 % of cholangiocarcinomas. There are only few cases in the literature.
Method: A 50-year old female presented with abdominal bloating and pain. Abdominal ultrasonography showed hipoechoic solid mass in the segment 4A. The serum level of CEA was 3.4, CA19.9 was 71.2, AFP was 1.78. Radiological and clinical findings were consistent with cholangiocarcinoma. A trucut biopsy was performed. Microscopically, there were findings consistent with squamous differentiation. Immunohistochemically, neoplastic cells were positive for p63, HMWCK,PanCK and negative for Hepatocyte-A. The trucut biopsy reported as tumour with squamous cell differentiation. Afterwards a tumour board decided for the left liver lobectomy. Macroscopically, there was solid nodular mass with 6x5x4.5 cm dimensions. Cut surface was creamy white color and elastic in consistency. Microscopically, the lesion was a malign neoplasm composed of squamous cells and glandulary structures. There were nuclear pleomorphism and necrosis. Immunohistochemically neoplastic cells displayed diffuse CK5/6,p63,CK7,CK19 and focally CEA expression. Arginase,Hepatocyte-A,Glypican-3 and CK20 were negative.
Results: The final diagnosis was ASC. The patient received chemotherapy and was alive without tumour at 9 months follow-up.
Conclusion: Diagnosis of ASC is very important due to its poor prognosis and rarity.

E-PS-09-007

Histopathological changes in livers of paediatric patients with urea cycle disorders who underwent liver transplantation

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Objective: Liver transplantation (LTx) is recommended for various metabolic diseases. Urea Cycle Disorders (UCDs) belong to this group. The aim of this study was to determine histopathological features suggestive of UCDs in livers removed from paediatric patients who underwent LTx.
Method: Material from livers of children with UCD who underwent LTx between 2008 and July 2016 were retrospectively reviewed. The following features were analyzed: the extent of fibrosis assessed according to two scales: METAVIR and Ishak; chronic inflammation graded according to METAVIR scale and steatosis (minimal up to 33 % of hepatocytes, moderate - 34–66 % of hepatocytes, significant >67 % of hepatocytes).
Results: In 9 (64.3 %) explanted livers histopathological changes such as hepatocytes with foamy, light tan-coloured cytoplasm and microvesicular steatosis were found. In 1 case (7.1 %) microscopic evaluation showed none - complete cirrhosis (METAVIR 3/Ishak 5), 1 liver was within normal, 1 organ presented only minimal steatosis and fibrosis (METAVIR 1/ Ishak 2). One patient underwent transplantation 3 times. In the second explanted liver of this patient, the features of complete cirrhosis (METAVIR 4/Ishak 6) were found.
Conclusion: There are no pathognomonic histopathological changes characteristic for Urea Cycle Disorders, however, hepatocytes with foamy, light tan-coloured cytoplasm and microvesicular steatosis should suggest this diagnosis.

E-PS-09-008

Staging and grading chronic viral hepatitis: How feasible in a tropical population

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Objective: To determined the epidemiological pattern and grade /stage all cases of chronic viral hepatitis using Ishaq Modified Histologic Activity Index (HAI)
Method: Ten year biopsies fixed in formalin, embedded in paraffin and stained with routine and special stains were reviewed. Data analyzed using SPSS Version 16.0
Results: Chronic viral hepatitis formed 55.2 % was the most common of liver diseases. There were119 male and 47 female with male to female ratio of 2.5: 1 and peaked in the 3rd decade of life. 42.2 % had modified Ishaq HAI score of 4–8, while 28.3 % and 27.1 % had score 1–3 and score 9–12 respectively. Only 2.4 % had score of 13–18. 70.5 % of cases were between stages 0–2, 25.9 % of cases were stage 3–4 while only 6 % were in stage 5. HBV was found in 77.7 % of cases, HCV; 13.3 % and HBV/HCV co infection in 9.0 %.
Conclusion: CVH was the commonest form of CLD, peaked in the 3rd decade of life. 42.2 % were in mild grade disease while 70.5 % had stage 2 and below disease. HBV infection was the most common aetiology

E-PS-09-009

A challenging diagnosis of well differentiated hepatocellular carcinoma arising in a telangiectatic hepatocellular adenoma. Case description and review of hepatocellular adenomas diagnosed and treated in our center

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Objective: Due to de diagnosis of a hepatocellular carcinoma (HCC) arising in a telangiectatic hepatocellular adenoma (THCA), we analyzed the epidemiological features and malignancy potential of 10 hepatocellular adenomas (HCA) surgically treated in our center (1991–2016).
Method: .
Results: In our series, tumour median size was 8,4 cm (range 3–18,5 cm), median age was 40 years with female predominance (90 %) and oral contraception (OC) in 80 %. The surgical indications were: symptomatic bleeding (30 %), size (10 %), suspicion of malignancy (50 %), multicentricity (10 %). Histologically, 90 % of HCA showed steatosis, 20 % were telangiectatic and 20 % had focal cytological atypia. THCA consisted of trabecular hepatocellular proliferation with short fibrous structures associated with thickened arterial walls and it harbored foci of well differentiated HCC. B-catenin immunostaining showed a diffuse membranous pattern without nuclear expression in all cases. Bleeding was associated with tumour-size >5 cm. Atypia and malignant transformation occurred in older patients (median age 67 years) without OC, in HCA >8 cm, with pseudocapsule and telangiectatic features.
Conclusion: Most THCA affects women with a history of OC; malignant transformation approaches 4,2 %. In our study, HCC arose in THCA of elderly woman without history of OC. Furthermore, atypia and malignant transformation occurred in older patients without use of OC, that should prompt adequate follow-up.
None

E-PS-09-010

Massive cardiac metastasis of hepatocellular carcinoma in a 36-year-old patient with a negative hepatotropic virological status

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Objective: Introduction: Hepatocellular carcinoma (HCC) is the most common primary hepatic tumour. HCC is usually secondary to liver cirrhosis but most commonly it develops in the course of HBV and HCV infection. The most common sites of metastases are lymph nodes, lungs and bones. Here, we present the case of a 36-year-old female with massive cardiac metastasis of HCC.
Method: N/A
Results: Case report: Ultrasound examination performed because of abdominal pain revealed a tumour in the liver, interpreted as focal nodular hyperplasia. Four months later the patient with cachexia due to persistent vomiting was admitted to the Department of Vascular, General and Transplantation Surgery, Wroclaw Medical University. CT scan exposed enlargement of the tumour and compression of the stomach. Partial resection of the liver was performed. Histopathological examination revealed texture of HCC. Control tests performed after several months showed bilateral adrenal masses, abnormal ECG and a nodular structure filling the right ventricle of the heart. Soon the woman died due to progression of cancer and heart failure.
Conclusion: Conclusions: Post-mortem histopathological examination confirmed the alleged metastatic nature of lesions in the myocardium. Although the incidence of HCC metastases to the heart is extremely rare, the possibility of their occurrence should be considered.

E-PS-09-011

Morphological background of intraoperative radiation therapy appliance to prevent locoregional progression in patients with pancreatic ductal adenocarcinoma

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Objective: It is well recognized that pancreatic ductal adenocarcinoma (PDAC) is associated with very poor prognosis, early locoregional invasion and distant metastases. One reason for this is the proliferation of tumour growth through perineural spaces.
Method: To evaluate the efficacy of intraoperative radiation therapy (IORT) for the extrapancreatic perineural invasion (EPn) in the development of locoregional recurrence in patients with PDAC.
Results: In 14.5 % (22/152) the tumour was pT1-2, pN0, extraPn 0, R0. R1 detected in 32.1 % (49/152). EPn1 was detected in 36.8 % of cases (56/152). Metastases in regional LN was found in 62.5 % (95/152) of cases. In the study of autopsy basic morphological parameters speakers include locoregional tumour progression and / or a distant progression. Locoregional recurrence was found in 85 % of cases (29/34), which is manifested by the presence of perineural invasion. The mean time from surgery until locoregional recurrence without EPn1 - 14 months, with the presence of EPn1 - 9 mon.
Conclusion: Thus, the absence of regional LN and/or with R1-status doesn't preclude the development of locoregional recurrence in patients with PDAC. This is what necessitates a combined approach to the treatment of these patients, including surgery, supplemented by conducting IORT that effectively influences on tissues and reduces the number of local recurrence.

E-PS-09-012

Vascularisation of focal nodular hyperplasia of the liver depends on its size

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Objective: Morphometric evaluation of the vascularization of different sizes focal nodular hyperplasia (FNH) of the liver.
Method: Studied surgical specimens of FNH, obtained from 15 patients. FNH nodules were divided depending on the size: small (S-FNH - d < 2 cm), medium (M-FNH - d = 2–5 cm) and large (L-FNH - d > 5 cm). On the histological specimens staining with hematoxylin and eosin, determined the number and total area of the arterial and sinusoidal lumens, and degree of tissue vascularity.
Results: The largest number of branches of bringing artery detected in the M-FNH. The total area of the lumens also had maximum value in the M-FNH: more on 3.2 % and 31.9 % ($p < 0.05$) compared to the S-FNH and L-FNH, respectively. The greatest number of sinusoids noted in the S-FNH: on 59.8 % and 107.4 % ($p < 0.01$) higher than in M-FNH and L-FNH, respectively. The total area of the sinusoidal lumens in S-FNH exceed those on 51.8 % ($p < 0.05$) in the M-FNH and on 110.3 % ($p < 0.01$) in the L-FNH. The degree of S-FNH vascularization -7.7 %, M-FNH - 5.7 %, L-FNH - 4.2 %.
Conclusion: The number and area of the arterial and sinusoidal lumens depend on the size of FNH. The degree of vascularization decreases as increasing sizes of FNH.

E-PS-09-013

Analysis of Mucin expression and DNA methylation in serous adenoma of the pancreas

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Objective: Serous adenoma of the pancreas is a relatively uncommon neoplasm. We aimed to analysis Mucin expression and methylation status of MUC promotor regions in serous adenoma.
Method: All tissue specimens were retrieved from the files of the Kagoshima University during the period from 2005 to 2014. 8 cases were available for further immunohistochemical examination. 3 cases were available for methylation status.
Results: The expression rates (more than 10 % of tumour cells stained) were MUC1, 37.5 %(3/8), MUC2, 0 % (0/8), MUC4, 0 % (0/8), MUC5AC 0 % (0/8), MUC6, 87.5 % (7/8) in the immunohistochemical examination. On the other hand, although hypomethylation status of MUC4, MUC4 mRNA was negative and no MUC4 positive staining in all 3 cases,In contrast, we found hypermethylated DNA in MUC1 and MUC2, and MUC1 and MUC2 negative mRNA.
Conclusion: We found discrepancy between MUC4 promoter demethylation status and mRNA or mucin expression in serous adenoma.

E-PS-09-014
Adenosquamous carcinoma of the pancreas: A case report
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Objective: More than 95 % of malignant neoplasms of the pancreas arise from exocrine glands. Ductal adenocarcinoma is the most common primary pancreatic malignant disease. Primary adenosquamous cell carcinoma (ASC) of the pancreas is very rare (accounts for 1–4 % of all exocrine malignancies) and aggressive. ASC is a variant of adenocarcinoma and defined as a tumour in which both glandular and squamous elements are histologically malignant.
Method: Fifty-eight years old man presented with dyspepsia. Positron Emission Tomography + Computed Tomography (PET/CT) showed 1,2X1 cm hipodens mass in the pancreatic tail. Tru-cut biopsy of the pancreatic mass was sent to pathology laboratory.
Results: At the microscopic examination, tumour exhibited a biphasic malignant growth identified adenocarcinoma and squamous cell carcinoma. The adenocarcinoma component contained ductal or glandular structures with focal to abundant intracellular or extracellular mucin, squamous differentiation was characterized by irregular and infiltrating nests or sheets of polygonal cells with distinct cellular borders, intercellular bridges, eosinophilic cytoplasm.
Conclusion: Pancreatic cancer originates mainly from the exocrine duct cells. Adenosquamous cell carcinoma of the pancreas is very rare. Nerve invasion can be found in almost all the cases It has a poor prognosis and short survival with any treatment. The principle treatments are surgery, radiotherapy and chemotherapy.

E-PS-09-015
Primary hepatic neuroendocrine carcinoma
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Objective: Primary neuroednocrine hepatic carcinoma (NHC) represent 0,3 % of neuroendocrine tumours. They are usually found in the right lobe of apparently normal livers and rarely do they cause a carcinoid syndrome.
Method: We present a 67 y/o male who presented a solid mass in the right hepatic lobule with no other lesions on imaging, gastroscopy or colonoscopy. A right hepatectomy was performed.
Results: The specimen enclosed an 18 cm multilobular, friable and well defined mass with necrotic areas. Microscopic study revealed blue neoplastic cells with round nuclei, arranged in rosette-like structures, as well as limphovascular invasion. With these findings , the primary diagnosis was of a neuroendocrine tumour, which when located in the liver is usually metastatic. An ample IHC panel was assigned in order to differentiate between aother less common metastatic tumours. The latter revealed CK7, CK8-18, sinaptophysin positivity and a proliferation rate of 40 %. An electron-microscopy study was also performed, displaying cytoplasmatic granules consistent with the neurosecretory type. The combination of histological, IHC and electron-microscopy findings, as well as the lesion's exclusive localization in the liver, lead us to the diagnosis of primary NHC.
Conclusion: Six months post-surgery, the patient continues to be disease-free on radiological follow-up.

E-PS-09-017
A case report: An unusual duet of liver diseases - diagnostic and treatment difficulties
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Objective: A 31-year-old woman was referred for treatment of chronic hepatitis C (CHC) with unusual high biochemical activity. We need to estimate morphologic and serologic changes before treatment.
Method: We evaluate HCV RNA viral load, AST, ALT, IgG, level of anti-nuclear antibody (ANA), F-actin antibody titer and liver histology.
Results: Physical examination was unremarkable. There were found elevated AST 465 U/L, ALT 603 U/L levels, HCV RNA viral load 1550000 IU/mL, IgG 2050 mg/dL, ANA titer 1:160 and F-actin antibody titer of 22 U. Liver biopsy revealed moderate portal infiltration consisting of lymphocytes with aggregate formation and numerous plasma cells. Interface hepatitis was severe with clusters of plasma cells. Lobular inflammation was moderate with apoptotic bodies and zone 3 confluent necrosis. Moderate portal and mild periportal sclerosis was revealed.
Conclusion: We revealed a chronic liver disease severe histologic activity with morphologic and serologic features of both CHC and autoimmune hepatitis (AIH). The patient was started on direct acting antiviral therapy with a prompt resolution of both the liver biochemistry and serologic features of AIH.

E-PS-09-018
Interleukin-6 Receptor influences cholangiocarcinoma progression
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Objective: Cholangiocarcinoma (CCC) is a malignant neoplasm originating from the biliary tree epithelium. Chronic inflammation is a main risk factor for CCC development. This process is, among others, regulated via the IL-6/IL-6R/JAK/STAT pathway which is supposed to be activated through either classic or trans-IL-6 signaling. Classic IL-6 signaling is guided by the membrane-bound Interleukin-6 receptor (IL-6R), whereas the soluble receptor mediates IL-6 trans-signaling. We hypothesize classic and trans-IL-6 signaling to differently impact the pathogenesis of cholangiocarcinoma.
Method: Survival analysis was achieved using data of The Cancer Genome Atlas. In vitro studies were performed using Tocilizumab, IL-6 and HyperIL-6. Immunoblotting and qRT-PCR was used to determine expression levels of proteins involved in the IL-6/IL-6R/JAK/STAT signaling pathway in five CCC cell lines and in patient derived tumour tissue.
Results: CCC cell lines and human tumour tissue express many proteins involved in solubilization of the IL-6R. Blocking the IL-6R using Tocilizumab decreased STAT3 phosphorylation, whereas IL-6 (via

classic-IL-6 signaling) and HyperIL-6 (via trans-IL-6 signaling) differently activated STAT3. The IL-6R is expressed in CCC patients and influences overall survival.
Conclusion: The results demonstrate that, targeting the IL-6/IL-6R/JAK/STAT pathway members play a crucial role in CCC which might open doors for novel therapeutic approaches.

E-PS-09-019
Primary pancreaticobiliary location of an uncommon neoplasm: A report of two cases
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Objective: Carcinosarcoma of the pancreaticobiliary tract is a rare entity comprising a small subset of all pancreaticobiliary neoplasms. This communication aims to highlight its histopathological and clinical features.
Method: We report two cases of carcinosarcoma primary located in the pancreaticobiliary tract.
Results: Both patients were 80 years old. They presented with abdominal pain and jaundice. Computed tomography scan showed abdominal masses. One patient had a cholecystectomy with a right hemicolectomy, the other had an extended pancreaticoduodenectomy. Histologicaly,the first patient was diagnosed with a carcinosarcoma of the gallbladder invading the right colon, the second had a carcinosarcoma of the pancreas.
Conclusion: Carcinosarcoma of the pancreaticobiliary tract is a rare entity comprising a small subset of all pancreaticobiliary neoplasms and very few clinical data and treatment options have been published.The tumour has cells recognizable as adenocarcinoma as well as a high-grade spindle-cell component. Each of these elements shows distinct immunohistochemical and ultrastructural characteristics.

E-PS-09-020
A rare case of synchronous small cell pancreatic and lung carcinoma, TTF-1 positive
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Objective: Thyroid transcription factor-1 (TTF-1) plays a crucial role in morphogenesis of the lungs and and for this reason is expressed in up to 90 % of pulmonary neuroendocrine cell carcinomas.
Method: There have been reports in medical bibliography of extrapulmopnary small cell carcinomas expressing TTF-1, approximatelly in 21–84 % of cases. This is why in such cases, a great diagnostic dilemma emerges weather a pulmonary tumour refers to a primary carcinoma or a metastatic one.
Results: We report the case of a 78-years-old man in whom a pancreatic mass was found. During endoscopy of the upper GI track biopsies were taken through duodenum and histological examination revealed a neoplasm with features of a small cell carcinoma, positive in TTF-1 and neuroendocrine markers. CT-scan revealed metastatic foci in peripancreatic lymph nodes, peritoneal cavity, adrenal glands and lung masses. Bronchoscopy was performed and biopsies revealed a neoplasm with features same as those described above.
Conclusion: TTF-1 expression in neuroendocrine tumours of the small-cell type are not uncommon at extrapulmonary locations. The case described, as others in bibliography, is suggestive of primary extrapulmonary carcinoma that express TTF-1. All these neoplasms in case of synchronous neoplasm with the same histology in lung are thought to be metastatic, not primary.

E-PS-10 Gynaecological Pathology

E-PS-10-002
Analysis of pap tests in Tepecik Education and Research Hospital as a quality control measure: An observational study
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Objective: The pap test is an efficient way of screening cervical abnormailties. It also can be used as a quality assurence factor. Objective of this study is to analyze pap smears according to patients' age, Ascus / SIL ratio, sufficiency of samples and diagnoses.
Method: In this study, 1010 smears which reported by 9 pathologists in september 2016, retrospectively analysed by IBM SPSS statistics 22.
Results: 1010 Pap tests were examined. Among them, there were 29 ASCUS, 2 LSIL, 90 atrophia. 444 of them had enfection. 17 samples were insufficient. Ascus/ SIL ratio were 14,5. After this diagnosies, 5 of the patients underwent control smear , 2 patients underwent hysterectomy and their results were benign. 3 patients underwent cervical biopsy and 2 of them rediagnosed as CIN1.
Conclusion: Ascus/SIL ratio generally has been used as a quality control measure. According to previous studies this ratio could vary from 0.6 to 4.5. In my study this ratio was 14.5. So this findings were not parallel to the literature. The short duration of the study, high ratio of infection may affect the results. As a result, additional precautions should be taken by my instution for better quality.

E-PS-10-003
Female adnexal tumour of probable Wolffian origin (FATWO): A case report
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Objective: Female adnexal tumours of probable Wolffian origin (FATWO) are rare epithelial tumours,first described by Kariminejad and Scully in 1973. FATWOs are currently regarded as potentially malignant lesions as 10 % of cases follow an aggressive course,usually when adverse prognostic features are present. Herein we present a case of FATWO.
Method: Description of clinicopathological and prognostic factors of a case of FATWO.
Results: 36-year-old woman,underwent laparotomy due to a right adnexal mass shown in ultrasonography. Intraoperatively, a 50 mm mass of the right broad ligament with adhesions to the right adnexa was found and resected, with capsular rupture. Macroscopic examination revealed a 49 g white encapsulated solid mass. Histologically, the lesion was composed of epithelioid and spindle cells arranged in sieve-like, trabecular and solid patterns. Immunoprofile: cytokeratines+,vimentin+, calretinin+ ,CD10+, MelanA+,inhibin+, EMA-,CD117-. Five months after diagnosis, hysterectomy was performed and residual tumour was found at uterine serosa. Additional treatments were not performed. At present, 24 months after diagnosis, the patient is alive without evidence of disease.
Conclusion: FATWO are rare tumours that can present a wide diversity of histological patterns. Surgery is the main treatment as the role of other therapies remains ill-defined. Long-term surveillance is advised since recurrences and/or metastasis can occur, especially when adverse prognostic factors are identified.

E-PS-10-004

Epithelioid trophoblastic tumour metastasising to lungs bilaterally: A case report and review of the literature

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Objective: Epithelioid trophoblastic tumours (ETT) of the uterus are very rare tumours that develop from chorionic-type intermediate trophoblasts. Here a very rare case of ETT and review of the literature is presented.
Method: A 44-year-old woman undergoing lobectomies of the lungs for ETT. The patient had suffered from choriocarcinoma at the age of 39 years, underwent total hysterectomy and recieved chemotherapy. Serum hCG levels were 11.3 mIU/mL the time between lobectomies. Two years after operation, pulmonary non-regressive cavitary lesions occurred bilaterally and had progressed in spite of chemotherapy. Lobectomies for bilateral pulmonary lesions were performed. Grossly, tumours were 6 and 4,5 cm in diameter, mostly cystic with tan solid areas consisting of hemorrhage and necrosis in centre. Histopathological evaluation revealed uniform trophoblastic cells arranged in cords and nests with eosinophilic/clear cytoplasm and round nuclei. Necrosis was present. Immunohistochemical examination showed that tumour cells were stained positively for hPL, hCG, cytokeratin18 and inhibin-a. Finally; histopathologic examination revealed ETT metastasizing to lungs bilaterally. Furthermore, hysterectomy material was examined retrospectively regarding these findings and revealed ETT cells adjacent to choriocarcinoma.
Results: No tumours or abnormal symptoms developed during the 4 month clinical follow-up.
Conclusion: ETT mostly affect women of reproductive age and are reported to metastasise to lungs. Misdiagnosis delays effective treatment and affects survival.

E-PS-10-005

An extraordinary occurence: Clear cell carcinoma of the fallopian tube associated with endometrioid carcinoma of the uterus

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Objective: Endometrial carcinoma is the most common gynecologic cancer in developed countries, with endometrioid carcinoma accounting for 60 % of all cases. At the other end of the spectrum, primary fallopian tube carcinoma is extremely rare, accounting for 0.14–1.8 % of all female genital malignancies. Clear cell carcinoma represents only 2 % of all fallopian tube carcinomas.
Method: We report the case of a 63-year-old female presenting to the University Emergency Hospital Bucharest for abnormal vaginal bleeding. The patient underwent radical hysterectomy with bilateral salpingo-oophorectomy and the specimen was sent to the Department of Pathology for evaluation.
Results: Histopathological examination revealed a FIGO stage IA endometrial endometrioid carcinoma, associated with a clear cell carcinoma, which was located and appeared to originate in the right fallopian tube, with no macroscopic or microscopic connection between them. Immunostaining for ER, PR, p53 and Napsin A suggested a completely different histogenesis and helped establish the final diagnosis.
Conclusion: Primary fallopian tube carcinomas are extremely rare tumours and their association with a synchronous malignancy of the genial tract is even more extraordinary. To our knowledge, this is the first report in the scientific literature of clear cell carcinoma of the fallopian tube associated with endometrial carcinoma.

E-PS-10-006

Histopathological evaluation of ovarian masses

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Objective: The aim was to study the histopathological patterns of ovarian masses.
Method: This is a retrospective cross sectional study performed at Department of Pathology, Patan Academy of Health Sciences, Nepal from April 2011 to March 2016.
Results: During the study period, 528 ovarian masses were operated at our institution. Among them, 399 cases (76 %) were neoplasms and 129 cases (24 %) were non-neoplastic lesions. Benign, borderline and malignant neoplasms were 89.7 , 1.8 and 8.5 % respectively. Benign neoplasms were more common in 21–30 years and malignant in 41–50 years age group. There were 156 (39.1 %) surface epithelial tumours, 236 (59.1 %) germ cells tumours and 6 (1.5 %) sex cord stromal tumours. Mature cystic teratoma, followed by serous cystadenoma was the most frequently encountered benign tumour. Serous cystadenocarcinoma was most prevalent in the malignant group.. Among the non-neoplastic masses, the most common was endometriotic cyst (55 %) followed by corpus luteal cyst (29 %).
Conclusion: Ovarian neoplasms are more common than non-neoplastic lesions. Mature cystic teratoma was the most frequently encountered benign tumour. Serous cystadenocarcinoma was most prevalent in the malignant group. Endometriotic cyst was the most common non-neoplastic lesion.

E-PS-10-007

Evaluation of the relationship between cervical intraepithelial neoplasia grades and connexin 43

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Objective: Cervical intraepithelial neoplasia (CIN) is a premalign cervical disease, also called cervical dysplasia or cervical interstitial neoplasia or cervical squamous intraepithelial lesion (LSIL). The microscopic features of CIN indicate an infection leading to normal differentiation and loss of maturation in the squamous epithelium.
Method: 79 cases were included in the study who were referred to the pathology department between 2014 and 2015 and who had cervical intraepithelial neoplasia (CIN) (grade 1, 2, 3). 41 of these cases had CIN 1. The average age of these women was 44.93 and the age range ranged from 31 to 66 years. 16 women were diagnosed with CIN2. The average age of these women was 42.06 and the age range ranged from 28 to 65. 22 women were diagnosed with CIN 3. The average age of the women was 48.87 and the age range ranged from 32 to 63 years. Sections of 3 micrometer thickness were taken from the paraffin blocks of the uterus on the polylysine slide. These sections were immunostained chemically with Cx43 antibody by ABC technique.
Results: Cells showing staining were evaluated as positive. It was noticed that it was stained in endocervical glands and that there was no staining in the squamous epithelium.
Conclusion: In this study, there was no staining in the dysplastic epithelium. No change was observed according to the degree of dysplasia.

E-PS-10-008

Adenomatoid tumour of the uterus: A case report

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Objective: We report a case of uncommon uterine adenomatoid tumour. It is a benign tumour of mesothelial origin with incidence of 1,2 % in hysterectomy.
Method: A 39-old woman with clinical diagnosis of uterine fibromatosis underwent surgery. Histopathological and immunohistochemical investigation was performed.
Results: Microscopically tumour presented as small gland-like structures interspersed within smooth muscle tissue. Immunohistochemically gland-like structures stained with Cytokeratin pan (AE1 and AE3). A MIB-1 expression was 0–1 mitoses per field of view, ×400.
Conclusion: Adenomatoid tumour of the uterus is an incidental finding during surgery performed for other causes. It shows immunohistochemical staining suggestive for its mesothelial origin. The prognosis is excellent.

E-PS-10-009
To study the histopathology reports of loop electrosurgical excision procedure (LEEP) of cervical transformation zone and to see its correlation with preprocedure cervical biopsy/ cytology, between 2011 and 2016, in our hospital
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Objective: To study the contents of the histopathology reports of LEEP cases, and to correlate with cervical biopsy/ cytology report, in our hospital between 2011 and 16.
Method: Our hospital records between 2011 and 16 yielded a total of 35 histopathology reports (34 patients). Their pre LEEP cervical biopsy, cytology reports were noted. Two cases did not have pre LEEP cervical biopsy/ cytology reports.
Results: The mean age was 48.9 years (median 58.5 years; age range 31–71). Out of 35 reports, two cases were submitted as outside blocks, and 34 reports mentioned that all the tissue was submitted. Deep cuts were mentioned in 12 cases. The diagnoses included 14 CIN II/III , 3 microinvasive squamous carcinoma, 1 squamous carcinoma, 1 adenocarcinoma in situ (AIS), 1 adenocarcinoma, 3 CIN I and 12 cervicitis. Six out of 20 CIN II/ III plus diagnoses showed margin positivity. Margin was not commented upon in one case of CIN II. The concordance between LEEP and cervical biopsy/cytology was 63.6 % (21/33 cases) for CIN II plus diagnoses. Discordance is recorded between CIN I and inflammation and also between CIN I and CIN II.
Conclusion: The concordance rate between LEEP and cervical biopsy/ cytology is 63.6 %, and shows a scope for improvement.

E-PS-10-010
Morphogenesis of placenta at endocrinopathies (diabetes and thyroid pathology) in mother
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Objective: Last years the endocrine diseases are the most important during pregnancy.
Method: 50 placentas of women with diabetes of 1 type, 91 placentas with thyroid pathology (56 with hypothyroidism, 35 with diffuse toxic goiter), 25 placentas with combination of these pathologies were researched. Light microscopy, raster microscopy with usage of micro- and macroanalysis, atomic-force microscopy were carried out.
Results: The villi of intermediate type with moderate vascularization dominated at pathology. The decreasing of square of villous tree was: hypothyroidism (52,1 ± 2,6 %), diffuse toxic goiter (44,0 ± 1,9 %), diabetes of 1 type (40,0 ± 2,3 %), combined pathology (45,0 ± 5,8 %), 62,5 ± 4,5 % in control group. The decreasing of blood vessels was in next sequence (12,6 ± 1,9 μm, 10,3 ± 1,6 μm, 9,8 ± 1,2 μm, 9,3 ± 1,1 μm and 28 ± 2,4 μm). The content of fibrinoid on villi increased in the same sequence. In separate sites the endothelial cells in all groups at pathology were smooth, atrophied and damaged.
Conclusion: The greatest changes in placenta were revealed at combined endocrine pathology, what can be a reason of particular alertness during pregnancy and childbirth.

E-PS-10-011
Atypical proliferative serous tumour of ovary with synchronous involvement by non Hodgkin diffuse large B-cell lymphoma CD5 positive: An unusual case report
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Objective: Although unusual ovarian involvement by lymphoma may either be primary or secondary.However the latter is much most common.Almost any type of lymphoma may occur in the ovary.Among these the most common are diffuse large B-cell,Burkitt and follicular lymphomas
Method: A 79 year old woman with a medical history of non Hodgkin DLBCL presented to our hospital with 2 month history of lower abdominal pain.Her pelvic/transvaginal ultrasound revealed a right ovarian cyst with a diameter of 3,5 cm. The patient underwent right salpingo-oophorectomy
Results: Histological examination confirmed a diagnosis of atypical proliferative serous tumour of ovary.In addition in the ovarian stroma islands of malignant neoplasmatic cells were observed.Immunohistochemical study showed that the lesional cells were positive for CD79a, CD20, CD19, CD22, and CD5 while there was negative expression of CD23, CD138, CD3, CD10, EMA, Chromogranin and synaptofysin.According to these findings a diagnosis of metastatic non Hodgkin diffuse large B-cell lymphoma CD5 positive was made
Conclusion: Although very rare ovarian involvement by lymphoma must be considered in differential diagnosis from other neoplastic processes such as dysgerminoma,undifferentiated carcinoma,small carcinoma and granulocytic sarcoma

E-PS-10-012
Expression and diagnostic value of CA-125 biomarker in endometriosis
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Objective: This study was aimed to estimate the fluctuation of the expression of the CA-125 biomarker, in patients suffering from endometriosis. Endometriosis is described as a benign disease that usually affects the inner reproductive system, as ectopic endometrial tissue. The disease is present in women of any age, but it's especially common after the menopause. This specific biomarker was used to differentiate between women suffering from endometriosis and those suffering from ovarian cancer.
Method: The sample pool for this project was 35 women between the ages of 28–60 (with an average age of 39+/−8 years) which were histologically diagnosed with endometriosis and the levels of the biomarker were estimated using an immunoradiometric test in vitro (IRMA). Measurement of the results helped in staging disease progression and finalizing the original diagnosis. The histological examination of the tissues from these cases was performed using routine staining hematoxylin and eosin (H&E).

Results: Considering 35U/ml as the base level for the marker, 2 values were found just below the base level, 32 values above the base level and just 1 value way above normal ranges. The histological analysis of the tissues showed, presence of endometrial glands with typical endometrial substrate, in multiple sections.
Conclusion: Taking into consideration all of the above , we came to the conclusion that we can determine the presence of endometriosis using the CA-125 biomarker, which is more reliable when used in combination with laparoscopic and histological analysis in order to wipe out false negative results.

E-PS-10-013
Vascular "pseudo invasion" in laparoscopic hysterectomy specimens: A diagnostic pitfall
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Objective: Total laparoscopic hysterectomy has been shown to be an effective and safe technique for endometrial carcinoma(EC). More recently, this procedure has been associated with vascular pseudoinvasion (VSI) in cases of low-risk EC
Method: In this study, we evaluated the cases of endometrioid carcinoma (grade 1 and superficially invasive according to the International Federation of Gynecology and Obstetrics) treated by laparoscopic hysterectomy (LH) to determine the incidence of this finding and to better characterize its histopathologic features
Results: VSI was detected only in large, thick-walled vessels in the outer myometrium or in ectatic vessels anywhere in the myometrium (no tumour was seen in small vessels); Histologically conspicuous fragments of tumour detached from the vascular wall were seen (in more than one vessel). In addition. All of the cases also showed fragments of tumour in artifactual clefts in the myometrium. Lymph node sampling and/or peritoneal cytology showed no tumour.
Conclusion: Pathologists need to be aware of this artifact to avoid misinterpretation of vascular invasion in these cases with its associated therapeutic and prognostic implications.

E-PS-10-014
Struma ovarii in our series with review of the literature and retrospective analysis
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Objective: Struma ovarii is a rare ovarian tumour that has been reported to represent 0.5–1 % of all ovarian tumours. First described by Von Klden in 1895 and Gottschalk in 1899, struma ovarii is the most common type of monodermal teratoma and comprises about 3 % of all ovarian teratomas. Most patients are in the reproductive years.
Method: A total of 9 cases of struma ovarii were rewieved retrospectively at the University of Mustafa Kemal (2006 to 2017). Patients age, surgical procedure, localisation of tumour were identified.
Results: The age of patients were between 36 and 75 (the mean age was 56.2). In all the cases, the management of struma ovarii was surgical removal. 6 tumours were located in right, 3 tumours were located in left ovary.
Conclusion: Struma ovarii is defined as ovarian goiter which comprises either entirely or predominantly thyroid tissue (>50 %). This also includes cases of mature teratoma with less than 50 % thyroid tissue but harboring thyroid-associated malignancy. The vast majority of struma ovarii are benign, but careful examination should be performed not to ignore thyroid-associated malignancies.

E-PS-10-016
Leiomyomatosis peritonealis disseminata in a nonpregnant woman
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Objective: Leiomyomatosis peritonealis disseminata is uncommon benign lesion. It is characterized by multiple small nodules composed of mature smooth muscle tissue distribute throughout the omentum and peritoneum in woman of reproductive age. Most cases are associated with pregnancy or oral contraceptive use.
Method: Thirty-six year-old female patient, gravida 0, presented with abdominal pain for 1 year duration. She hadn't use oral contraceptive. Computed tomography revealed the mass that was completely filling the pelvis and extended to peritoneum.She has undergone laparotomy to remove the mass.The laparotomy revealed multi nodular solid mass ,which has originated in the anterior serosal surface of uterus.
Results: The macroscopic examination of the solid mass was 30x24x8 cm in size. The cut surface showed small nodules; appeared gray-white in color. The microscopic examination revealed nodules; composed of bland smooth muscle cells as ordinary leiomyoma without atypia and mitosis.Tumour cells were reactive for estrogen receptor, progesterone receptor, desmin, caldesmon on immunohistochemistry. We diagnosed the patient as 'Leiomyomatosis Peritonealis Disseminata '
Conclusion: We are presenting a rare case of leiomyomatosis peritonealis disseminata that is described in a nulligravida patient who hasn't use oral contraceptive.

E-PS-10-017
Primary uterine diffuse large B-cell lymphoma (PU-DBBCL): A case report with review of literature
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Objective: Primary uterine lymphoma is a rare neoplasm, accounting for 0,05 % of all uterine malignancies. Less than 70 cases have been reported. DLBCL is the most common subtype. We describe a case of PU-DLBCL.
Method: We received for consultation the material of endometrial curettage from a 36-year old HIV(+) woman presented with dysfunctional uterine bleeding. The initial diagnosis, based on a limited immunohstochemical study, was undifferentiated endometrial stromal sarcoma. A second endometrial curettage for an endometrial polypoid mass of 8,34 mm, accompanying with pelvic lymph nodes excision, was performed. A combined chemotherapy (R-CHOP) was administered. After a 2 year follow-up period, the patient is without signs of disease.
Results: On histology, endometrial stroma was diffusely infiltrated by large lymphoid cells with centroblastic morphology. Frequent mitotic figures, apoptotic bodies and necrosis were observed. Tumour cells were immunoreactive for LCA, CD10, CD20, BSAP, Bcl2 Bcl6, MuM1. Pelvic lymph nodes were uninvolved. Thorough clinical and imaging investigation showed no evidence of extra- uterine disease. A final diagnosis of PU-DLBCL was concluded.
Conclusion: PU-DLBCL represents a rare malignancy. Both gynaecolgists and pathologists should be familiar with the features of isolated genital tract lymphoma as patients can experience delay in diagnosis and misdiagnosis.

E-PS-10-018
Lipoleiomyoma with chondroid metaplasia of the uterus: A rare presentation of a benign tumour
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Objective: Uterine lipoleiomyoma is a rare benign tumour composed of variable amounts of smooth muscle, fat cells and fibrous tissue. Chondroid metaplasia in an uterine lipoleiomyoma is extremely rare with only a few reports in medical literature.
Method: We report the case of a 39-year-old patient who presented with pelvic pain. Ultrasound scan and MRI of the pelvis showed multiple circumscribed intramural or submucosal tumours of the uterus with maximum diameter 5 cm and heterogeneous appearance. She underwent laparotomy with excision of 6 of the tumours.
Results: Microscopically, the largest tumour revealed an admixture of smooth muscle fibers with mature fat cells in varying proportions, and scattered nodular areas of mature cartilage. No cytologic atypia, mitoses or necrosis were found in each counterpart of the tumour. Immunohistochemically, the fat and the chondroid cells expressed S100 protein and variably estrogen and progesterone receptors. The patient 1 year later is in good condition, with no evidence of recurrence. The rest of the tumours represented typical leiomyomas.
Conclusion: In conclusion, we report an extremely rare case of mature lipoleiomyoma with chondroid metaplasia of a leiomyomatous uterus. It is considered a benign tumour and is important to differentiate its different components from their malignant counterparts.

E-PS-10-019
Uterine malignant perivascular epithelioid cell tumour with late pulmonary metastasis
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Objective: Perivascular epithelioid cell tumours are rare mesenchymal neoplasms with a distinct perivascular epithelioid cell differentiation. They can arise in a large spectrum of anatomic locations, and are characterized by their myelomelanocytic phenotype and unpredictable natural history . A case of malignant perivascular epithelioid cell tumour (PEComa) of the uterus with late pulmonary metastasis is presented.
Method: A 60-year-old female patient admitted by obstetrics and gynecology department, complaining of lower abdominal pain and abnormal uterine bleeding. MRI revealed a 13-cm-mass located in subserozal space of uterine fundus, which is extending to the cervix uteri. Hysterectomy was performed.
Results: Histologically, the tumour was composed of round to polygonal cells with round nuclei and abundant clear to slightly eosinophilic cytoplasm. There were scattered foci of necrosis. The tumour cells showed high atypia and high mitotic activity (>50MF/10HPF). Immunohistochemically, the tumour was strong positive for HMB45, vimentin, B-katenin and p16. Focal positive for CD10 and desmin. The tumour was negative for S100, SMA, MSA, EMA, myoglobulin, inhibin, CD117, Melan-A, and CD68 . After surgery, the patient underwent three sessions of adjuvant chemotherapy. After 2 years, a 5 cm solitary metastatic mass was detected in right lower lobe of lungs, and lobectomy was performed. The tumour was arranged in nests or trabeculae of epithelioid cells with clear cytoplasm and round nuclei with prominent nucleoli and share same immunohistochemistry with the primary tumour.
Conclusion: Although PEComas have a wide spectrum of biological behavior, tumour size (>5 cm), infiltrative growth pattern, high nuclear grade, necrosis and high mitotic rate > 1/50 HPF are related with aggressive clinical behavior and poor clinical outcomes/prognosis.

E-PS-10-020
Solitary luteinised follicle cyst of pregnancy: Two cases
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Objective: Solitary luteinized follicle cyst of pregnancy (SLFCP) is a benign condition that affects pregnant females or appears during puerperium. It is self-limited in nature and most often regresses spontaneously in the puerperium.
Method: Two cases of SLFCP were described with clinicopathologic findings.
Results: The first case occurred in a 35-year old woman who was found to have a left ovarian mass during the caesarean section. The ovarian mass was removed by oophorectomy. The specimen has unilocular, thin-walled, clear fluid filled cyst measuring 13 × 9× 5 cm. Internal surface of cyst was smooth and solid tissue or papillary tumour was not seen. The ovarian tissue was measured as 3x2x1 cm adjacent to cyst. Microscopically, cyst was lined by luteinized cells with focal large nuclei, scattered nests of luteinized cells in the edematous fibrous wall. Mitotic figures were not seen. The patient has been healthy without disease after 15 years. The second case was a 26-year old pregnant woman who was found to have a right ovarian cyst during the caesarean section. The patient delivered a full term healthy female infant and the ovarian mass was removed by cystectomy. The specimen showed a unilocular, thin-walled, clear fluid filled cyst measuring 8 cm in diameter. Microscopic features were similar to the first case. No mitoses were identified, too. The patient has been healthy in 2 months after surgery.
Conclusion: The differentiation between solitary luteinized follicle cyst and a cystic ovarian tumour is important. Awareness of this entity will minimize the risk of a misdiagnosis.

E-PS-11 Haematopathology

E-PS-11-001
Myeloid sarcoma of the breast: An uncommon presentation
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Objective: Myeloid sarcoma is an extramedullary solid neoplasm of immature myeloid cells. Affected sites include skin, lymph nodes, bone, small intestine, and less commonly, the breast. These tumours usually develop synchronously or following the diagnosis of acute myeloid leukemia (AML).
Method: Core biopsy of the lesion was performed. The section were stained with routinary H&E. Immunohistochemistry was performed.
Results: A 27-year-old female presented with a lump in the left breast to our hospital. Computed tomography scan showed a mass in the left breast .Histopathological examination revealed a tumour composed of blasts with scant cytoplasm and round-oval nuclei. The tumour cells were immunonegative for cytokeratin, ER, PR, e-cadherin, Her2neu, CD3 and CD20. Malignant cells were immunoreactive for myeloperoxidase CD34, leukocyte common antigen (LCA) and lysozyme. These results established a diagnosis of myeloid sarcoma. Following the diagnosis of myeloid sarcoma bone marrow aspiration & biopsy was performed. The bone marrow was hypercellular with extensive blast infiltration consistent with AML.
Conclusion: Myeloid sarcoma is an uncommon neoplasm of immature myeloid cells. The breast is an uncommon site for presentation of this tumour. It is important to pathologists not to misidentify this tumour as lymphoma or carcinoma.

E-PS-11-002
Hodgkin lymphoma: A definite diagnosis to an indefinite clinical setting
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Objective: Hodgkin lymphoma (HL) is a lymphoid neoplasia with various clinical presentations. Non-necrotizing granulomas are frequent, whether in the context of sarcoidosis-lymphoma syndrome (SLS), in which sarcoidosis precedes lymphoma by 18–24 months, or sarcoid-like reactions, which can inclusively occur in non-regional tissues; additionally, about 16 % of organizing pneumonias (OP) arise from lymphoma. We present a HL case with a unique clinical presentation.
Method: A 58 year-old female complaining of dry cough presented sizable lung nodules; the consequent biopsy disclosed an OP pattern. Despite immunosuppressive therapy, the radiological profile aggravated throughout the following months; the repeat biopsy revealed an exuberant non-necrotizing granulomatous inflammation, suggesting sarcoidosis. Immunosuppression was reinforced but yet unable to hinder progression to generalized lymphadenopathies and hepatosplenomegaly. A retroperitoneal lymph node core biopsy was performed.
Results: The 4 mm sample portrayed an inflammatory infiltrate and scattered medium to large cells, rarely exhibiting proeminent nucleolus, occasional halos, and a CD30+, CD15+, CD79a+, CD45- and CD20- immunoprofile. Despite the sample scarcity, a presumptive diagnosis of classical Hodgkin lymphoma was established and agreed upon multidisciplinary consensus; suitable chemotherapy rendered immediate improvement.
Conclusion: To our knowledge, this is the first case of a lymphoma—namely HL—presenting in the setting of both a SLS and an OP.

E-PS-11-003
A retrospective clinicopathological and immunohistochemical study of benign cystic lesions of the spleen
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Objective: The aim of our study was to assess the characteristics and the types of benign cystic lesions of the spleen and to evaluate their immunohistochemical profile.
Method: We analysed all the benign cystic lesions of the spleen diagnosed between 2008 and 2017 in our Pathology Department. Routine histopathological diagnosis was supplemented by immunohistochemical analysis using the following markers : CKAE1/AE3, HBME-1, CD31, CD34, p63 and calretinin.
Results: Out of the 12 cases of splenic benign cystic lesions, divided by morphological features into parasitic and nonparasitic cysts, we found 6 echinococcal cysts , 4 epithelial cysts and 2 mesothelial cysts. The clinical diagnosis is not difficult for the echinococcal cyst, because is a zoonotic parasitic disease. The nonparasitic cysts are a rare condition that represent 10 % of all benign splenic cysts and their management is controversial: cystectomy, fenestration, percutaneous drainage and post-splenectomy sclerotherapy. Using IHC markers, the 2 mesothelial cysts are positive for anti-CKAE1/AE3, HBME-1 and negative for CD31, CD34; the 4 epithelial cyst are positive for CKAE1/AE3 , p63 and negative for calretinin.
Conclusion: The benign cystic lesions of the spleen are very rare, the majority of the lesions diagnosed were parasitic cysts. The exact nature of these lesions is the prerogative of morphological examination, which must sometimes be supplemented by IHC investigations.

E-PS-11-004
Simultaneous presentation of acute myeloid leukemia and chronic lymphocytic leukemia like lymphoid proliferation
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Objective: The simultaneous occurence of chronic lymphocytic leukemia (CLL) and acute myeloid leukemia (AML) has been rarely reported. Most of the cases are patients who have been treated for CLL. We present a very rare example of simulteneous presentation of AML and CLL like lymphoid proliferation.
Method: Bone marrow biopsy of 66 year old man who presented with weakness was evaluated. Immunohistochemistry was performed to formaline fixed parafine embedded tissue sample.
Results: CBC revealed pancytopenia. WBC count was 2,2x103mL of which 64,9 % was lymphocytes. The peripheral blood smear revealed incresed small lymphocytes. The bone marrow biopsy was hypercellular with infiltration of two distinct cell population. Nodular infiltration of small lymphocytes were accompanied with diffuse infiltration of blastic cells. Immunophenotypicaly small lymphocytic nodular infiltration areas were consistent with CLL/SLL, whereas diffuse infiltrative blastic areas were consistent with AML-M6.
Conclusion: The coexistance of CLL/ SLL and AML has been occasionally reported. The majority of them occurs after treatment of CLL with cytotoxic drugs. Hence they are thought to be secondary leukemia. Cases in the absence of prior treatment are exceedingly rare. Furthermore coocurrence of CLL like infiltration and AML-M6 is an extremely rare event.

E-PS-11-005
Primary hepatic marginal zone lymphoma (malt-type lymphoma). A case report
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Objective: The purpose of the study was to report an unusual lymphoid proliferation occurring in the liver of a 76-year-old woman without underlying chronic liver disorder or autoimmune condition.
Method: The patient refered to biliary symptoms, weight loss, sweating and pruritus. Tomographic study showed hepatic right lobe image of 9 cm that was resected (partial hepatectomy). Morphological and immunohistochemical study was performed.
Results: Histological sections revealed a dense population of small lymphoid cells with round nucleus and inconspicuous nucleolus, scarce large immunoblastic cells and numerous plasma cells in a stroma with sclerosis. The lymphoid proliferation showed some lymphoepithelial lesions of biliary ducts. Immunoprofile was CD20+ CD79a + BCL-2+, negative for CD3, CD5, CD23, CD45Ro and BCL-6, with a low Ki-67 index (5 %). Bone marrow biopsy was not involved and ulterior gastric biopsy had Helicobacter pylori gastritis.
Conclusion: Hepatic MALT-type lymphoma case studies have been rarely reported. This lymphoma is usually related with inflammatory or autoimmune diseases but there may be no underlying associations like in our patient at the time of diagnosis. Complete surgical excision in localized disease have been proposed. Although MALT-type lymphoma of the liver is considered a low grade lymphoma, patients should be closely followed up for recurrence.

E-PS-11-006
CD20 and Cyclin D1 expression in multiple myeloma
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Objective: CD20 and Cyclin D1 expression were reported at different rates in patients with multiple myeloma. The importance of this B-cell antigen for plasma cells is still unknown. This study aimed to investigate CD20 and Cyclin D1 expression of myeloma cells in bone marrow.
Method: Fourteen patients who were admitted to the hematology clinic with the diagnosis of multiple myeloma according to the criteria of the

"International Myeloma Working Group" were enrolled in this study. Age, gender, and the distribution pattern and positivity of CD20 and cyclin D1expression on multiple myeloma cells in bone marrow were evaluated.
Results: Twenty-one percent of cases express CD20 and 14 % express cyclin D1 which is in agreement with the results of the literature. The expression of CD20 was associated with a particular "lymphocytoid" morphology and the expression of cyclin D1 was associated with massive medullary infiltration.
Conclusion: CD20 and Cyclin D1 may have a prognostic influence in patients with multiple myeloma

E-PS-11-007
Diffuse large B-cell lymphoma occurring in a patient with lymphoplasmacytic Lymphoma/Waldenstrom macrogloblinemia
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Objective: Lymphoplasmacytic lymphoma/Waldenstrom macrogloblinemia (LPL/WM) is a low-grade lymphoma. Diffuse large B-cell lymphoma (DLBCL) reportedly occurs in approximately 13 % of LPL/WM cases.
Method: A 51-year-old man was followed for cold agglutinin disease and mild anemia. The patient had general malaise and dyspnea on exertion for 2 months, and was worse in the past month.
Results: CT scan and FDG-PET revealed hepatosplenomegaly and multiple lymphadenopathy including cervical lymph nodes. Lymph node SUVmax by FDG-PET was 6.2. The initial clinical diagnosis of WM/LPL was based on the elevated IgM level and symptoms of hyperviscosity syndrome. Immediate plasma exchange therapy improved the clinical symptoms and IgM levels. The clinical course was more rapid than that of the typical LPL. Pathological diagnosis of DLBCL with plasma cell differentiation was based on large lymphoid cell proliferation in lymph node specimen and additional immunohistochemistry analysis.
Conclusion: Both of clinical and pathological diagnosis suggested "DLBCL occurring in a patient with LPL/WM". Histological transformation in patients with LPL/WM is rare, but the frequency is the highest for DLBCL. However, there are case reports of transformation to HL or PBL. Transformation of LPL/WM has a prognosis similar to that of DLBCL and a 40 % chance of surviving 5 years.

E-PS-11-008
Mantle cell lymphoma cervico-facial location
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Objective: Mantle cell lymphoma (ML) is a rare non-Hodgkin lymphoma that accounts for 2–10 % of lymphomas. It affects adults of middle or advanced age, with male predilection. Clinically, it is often manifested as a disseminated disease with splenomegaly, medullary invasion and particular tropism for the digestive mucous. A revealing facial or cervical localisation is rarely found. We describe 2 new Tunisian cases.
Method: Two male patients aged 64 and 48 years, consulting for dysphagia and cervical mass. Physical examination reveals an indurated and painful swelling of the left amygdale in the first patient and magma of cervical and axillary adenopathies in the second.
Results: Histopathological examination revealed a diffuse lymphoid proliferation, made of small cells, with irregular nuclei, without visible nucleolus. The immunohistochemical study showed a positivity of CD20, CD5 and cyclin D1. CD10 and CD23 were negative. The two patients had chemotherapy,with Rituximab in the 2nd patient. Out comes were favorable in both patients, with no evidence of relapse.
Conclusion: The diagnosis of mantle cell lymphoma is anatomopathological and immunohistochemical. Cervical involvement is found most often in advanced stages of the disease, but may be the presenting sign as in the case of our patients.

E-PS-11-009
Thyroid lesions with marked plasmacytic differentiation: A two case report
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Objective: Introduction/Aim: Head and neck lymphomas have distinctive epidemiologic and clinicopathologic features including an association with immunosuppression, infectious organisms or autoimmune disorders. Lymphomas of the thyroid gland constitute up to 5 % of thyroid neoplasms. Primary thyroid lymphoma is an uncommon thyroid malignancy.The most common type of lymphoma in the thyroid gland, followed by MALT lymphoma (10–30 %). The treatment modalities significantly differ from other thyroid malignancies. Frequently it is accompanied by Hashimoto's thyroiditis, and it may be difficult to differentiate the two entities histologically.
Method: Case report: We present here two cases of incidental lesions of thyroid gland showing lymphoplasmacytic infiltration with the formation of germinal centers, destruction of the normal thyroid follicular architecture, Hürthle cell changes.
Results: The lymphoplasmacytic infiltration in both cases were positive for CD79α, and negative for CD20 and PAX5, there was no aberrant expression of CD56, cyclin D1, CD5, CD10, and CD43
Conclusion: Conclusion: Plasma cell differentiation is found in approximately one third of MALT lymphomas and is often accompanied with the production of monoclonal immunoglobulin with prominent plasma cell differentiation that can mimic plasmacytoma.The differential diagnosis between a plasmocytoma and a MALT lymphoma with marked plasma cell differentiation may be tricky, as they may have a similar histological appearance and both may arise in chronic thyroiditis backgrounds.

E-PS-12 Head and Neck Pathology

E-PS-12-001
Prevalence of Human papillomavirus (HPV) associated oropharyngeal squamous cell carcinoma (OPSCC) in Hungary
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Objective: Increasing prevalence of human papillomavirus (HPV) in oropharyngeal squamous cell carcinoma (OPSCC) has been reported in Europe. In OPSCC, expression of tumour suppressor p16 is used as a surrogate marker of HPV infection and has prognostic value. We aimed to investigate the epidemiology of OPSCC in our institute.
Method: 141 surgically removed or biopsy specimens were analyzed from the oropharyngeal region. Immunohistochemical (IHC) reaction for p16 was carried out in 141 cases of formalin fixed paraffin embedded material to identify HPV-positive OPSCC. Results were evaluated semi quantitatively.
Results: Patients were aged between 38 and 88 year (mean 62 year), the male to female ratio was 106 and 35 respectively. Tumour specimens from 43 of 141 (30,5 %) patients were classified as p16-positive and 98 (69,5 %) were p16-negative based on IHC analysis for p16 by qualified pathologists. Both p16-positive and negative tumours were

predominantly found in the tonsillar area and posterior part of the tongue. 88 % of p16-positive OPSCC was found to be poorly differentiated whereas 42 % of p16-negative tumours were found to be moderately-differentiated.
Conclusion: The prevalence of HPV associated oropharyngeal carcinoma is 30 % in our institute. The majority of them are poorly differentiated tumour. HPV associated carcinoma was most prevalent among men age 55 to 64 years, the three-fold higher OPC rates was seen among men versus women.

E-PS-12-002
Head and neck rhabdomyosarcomas: Report of 3 cases
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Objective: Rhabdomyosarcomas are rare malignant soft tissue neoplasm arising from myogenic cells and occurring more frequently in the childhood. The most commonly affected sites are the head and neck and genitourinary system. Our purpose was to analyze clinical, pathological, immunohistochemical features of 3 cases of head and neck rhabdomyosarcomas.
Method: We report 3 cases of head and neck rhabdomyosarcomas which were retrieved from the archives of Department of Pathology at Salah Azaiez Institute of Tunis. Radiologic findings and clinical history, as well as pathologic findings from hematoxylin and eosin slides and immunohistochemistry for myogenic markers were reviewed.
Results: Two of the three patients were adults in the sixties presented an obstruction of the left nasal cavity. The third one was a 3 years old child and presented a mass of the left jaw with ptosis. computerized tomography showed a tumour mass respectively in the nasal cavity, the maxillary sinus and the jaw. A biopsy was done for three of them which confronted to immunohistochemical stainings concluded in all of these 3 cases to an embryonal rhabdomyosarcoma. Adults were proposed to chemical therapy, radical sergery and external radiotherapy but the child had only chemotherapy.
Conclusion: rhabdomyosarcomas occur frequently in children and adolescents, and has been well studied in that population. In contrast, it is rare in adults and is not as well characterized clinically and pathologically.

E-PS-12-003
A randomised phase II study to evaluate the efficacy and safety of chemotherapy (CT) vs Androgen Deprivation Therapy (ADT) in patients with recurrent and/or metastatic, Androgen Receptor (AR) expressing, Salivary Gland Cancer (SGC)
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Objective: Among more than 20 histotypes of SGC only salivary duct carcinoma and adenocarcinoma NOS expresses AR. This represents a diagnostic challenge. This study (NCT01969578) aims to evaluate the efficacy and safety of ADT (experimental arm) vs chemotherapy (standard arm) in patients with recurrent and/or metastatic, AR expressing SGC by demonstrating a 15 % improvement in PFS rate at 6 months in favor of ADT.
Method: In this multicenter, randomized, phase II intergroup study treatment naïve patients (Cohort A) will be randomized to receive ADT or platinum-based chemotherapy. Previously treated patients will be enrolled in Cohort B will receive ADT. Patients randomized to chemotherapy can enter Cohort B at disease progression. Central testing of AR expression is based on staining intensity (0 = negative to 3 = strong) and percentage of positive nuclear stained cells (0 = =10 % to 3 = =70 %). AR expression requires a total score of 6. Mechanisms of AR activation and resistance will be studied.
Results: Currently, 31 patients are registered; 16 have AR expression and 11 have been randomized.
Conclusion: Identification of AR as a target for new treatment strategies in SGC can be practice changing. This academic study to explore new treatment options in SGC is an important step forward.

E-PS-12-004
Osteoclast-type giant cell tumour of parotid gland
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Objective: Osteoclast-type giant cell tumours (GCT) of salivary gland, similar to GCT of bone, are rare (<30 cases reported), but their histogenesis is not clarified as yet. In the largest series of 15 cases, an epithelial origin for these tumours was postulated with the conclusion that GCT is a poorly differentiated carcinoma, excluding a relation to GCT of the bone. Follow up studies suggest GCT can harbour a differentiated carcinoma.
Method: We present a case of GCT of parotid gland with low grade carcinoma in a 29 year old lady.
Results: The 18x10mm mass appeared solid-cystic with focally keratin + mononuclear spindle and CD68+ osteoclast-type giant cells admixed with keratin + low grade carcinoma and foci of osteoid and chondroid differentiation.
Conclusion: GCT is not included in the WHO classification, 2017; but is a distinct type of tumour of salivary gland and it should be included. Our observation and that of more recent studies do not confirm it as a type of high grade carcinoma. When reporting a GCT of salivary gland, an emphasis should be placed on the fact that the epithelial component may be low grade carcinoma.

E-PS-12-005
Rare malignant tumours of the larynx: Report of three cases
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Objective: We herein present three rare cases of uncommon malignancies that occur in the larynx
Method: The first case is of a 55-year-old man with long standing Ig D myeloma who presented with dry cough and breathlessness of 6 months' duration. The second case concerned a 69-year- old man admitted with chronic dysphonia. The third case concerned a 54-year-old man who presented with hoarseness with gradual onset of shortness of breath. In all the cases laryngoscopy revealed a suspected laryngeal mass.
Results: Respectively, in the first case histopathological examination on biopsy as well as immunohistochemistry led to the diagnosis of extramedullary plasmacytoma The patient was successfully treated with primary radical radiotherapy and showed no signs of local recurrence after 4 years follow-up. In the second case, the diagnosis of sarcomatoid carcinoma was made thanks to histological examination and immunohistochemistry on biopsy. A laryngectomy was performed. During the follow-up, a tumour recurrence occured within 6 months. In the last case, microscopic features on biopsy were consistent with the diagnosis of grade II differentiated chondrosarcoma. The patient had a laryngectomy.
Conclusion: The rare tumours of the larynx discussed in this report present unique characteristics. Because these tumours are uncommon, treatment parameters are less de_ned.

E-PS-12-006

Oncocytic Schneiderian papilloma: Review of four cases

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Objective: To evaluate the clinical and pathological features of sinonasal OSP highlighting the characteristic elements enabling distinction between OSP and the two other schneiderian papilloma subtypes.
Method: A retrospective review was performed of cases diagnosedwitn OSP in our department of pathology, between 2011 and 2017.
Results: Four male patients with OSP were identified.Age ranged between 56 and 80 years oldand nasal obstruction was found in all patients.OSP arose on the lateral nasal wall in three cases and in the right maxillary sinuse in one case. The diagnosis of inverted papilloma has been raised by the clinician in two patients.In all cases, pathological examination revealed polypoid lesions exhibitting exophytic and endophytic patterns with several layers of pseudostratified columnar cells containing uniform small dark round nuclei and eosinophilic cytoplasm,resembling oncocytes. The epithelium characteristically contained numerous small cysts filled with mucin or neutrophils.The presence of both exophytic and endophytic patterns of growth,the diffuse oncocytic nature of the epithelium and the minimal epidermoid component distinguished OSP from the other sinonasal papillomas.
Conclusion: Due to the possible recurrence of OSP and the eventual development into a malignant tumour,an accurate diagnosis and a regular follow-up are important.

E-PS-12-007

Spindle cell lipoma of the oropharynx - case report

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Objective: Lipomas are benign mesenchymal neoplasm that can arise anywhere, more commonly in soft tissue. They are rare in oral cavity, accounting for 1–4 %, and can present as many variants, including a spindle cell lipoma (SCL), first described in 1975.
Method: Male, 48-years-old, with complains of chronic tonsillitis and mass in left tonsil, clinically interpreted as a cyst, submitted to bilateral tonsillectomy.
Results: Gross examination revealed a polypoid mass with 2.2x0, 9 cm, pedunculated, attached to the left tonsil. Histologically it corresponded to a proliferation of mature adipocytes, with peripheral and small nuclei, intermingled by fibrous septae with spindle cells without atypia, positive for CD34, providing the diagnosis of SCL of the tonsil. Tonsils showed chronic tonsillitis, with agudization.
Conclusion: SCL are a very rare lipoma variant, usually presenting in the posterior neck, shoulders and back. In the oral cavity SCL are very rare, with less than 50 cases described in the literature, being the more common place the tongue. As far as we know this is the first case of SCL in the tonsil. Surgical excision is the treatment of choice with good results.

E-PS-12-008

Basaloid squamous cell carcinoma (SCC) debuting as metastatic carcinoma of unknown origin: Unusal tumour with unusual presentation and unusual localisation

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Objective: Basaloid squamous cell carcinoma (BSCC) is a rare tumour in the laryngeal region. It has often reached advanced stages with regional lymphatic metastases at the time of diagnosis.
Method: 56 y/o male debuts with palpable left cervical lymphadenopathy. On fibrobronchoscopy, a minute lesion in the Right Vocal Chord (RVC) was observed. A biopsy of the RVC mass and left cervical lymphadenectomy were performed. The former revealed a moderate dysplasia. A lymphatic nodule, containing a BC macrometastasis, was dissected during the lymphadenectomy. A captating lesion at the level of right piriform sinus was then identified in PET-TAC. New biopsy was performed and sent to us for histological examination.
Results: On routine H&E stains, patchy areas of diplastic squamous epithelium were observed with sharply demarcated nodules and trabeculae of basaloid cell proliferations, containing basal membrane matrix, in the immediate proximity. The latter exhibit moderate-to-severe cytological atypia and increased number of mitoses. Immunohisochemical studies showed diffuse reactivity for p63. The Ki-67 index was 90 %. A BSCC was diagnosed. The patient received adyuvant chemo- and radiotherapy and is currently disease-free.
Conclusion: We consider this case to be of interest, due to the unusual presentation of this rare neoplasm as a contralateral metastatic carcinoma of unknown origin.

E-PS-12-009

Genetic profiling of second primary tumour and field cancerisation of a female patient

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Objective: The squamous cell carcinoma is the most common malignancy developed in the oral cavity with a low survival rate. Second primary tumours are seen around 10–35 % of patients. Multifocal areas of precancerous alterations may trigger this process due to prolonged exposure to carcinogens.
Method: We present a case report of metachronous tumours and field cancerization in a heavy smoker, 64-year-old female. She presented with a maxillary squamous cell carcinoma in 2012, mild dysplasia on lateral of the tongue in 2014, and squamous cell carcinoma on the tongue with severe dysplasia on neighbouring epithelium in 2017.
Results: The patient underwent surgical resection of the maxillary tumour with free of surgical margins and had radiotherapy, no recurrence so far. Partial glossectomy and neck dissection were performed for the second tumour.
Conclusion: While the clinical follow-ups and managements are going through, next generation sequencing was applied to study 28 different genes including TP53, EGFR, CDK4, CDKN2A, and PTEN from both tumour samples and adjacent dysplastic epithelium to investigate the alterations the state of the epithelium, making it susceptible to developing a multifocal carcinoma.

E-PS-12-010

Mucoepidermoid carcinoma of the external auditory canal: Case report

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Objective: Ceruminous adenocarcinomas are rare malignant tumours, accounting for <2.5 % of all external auditory canal neoplasms, arising from the ceruminous gland of the external auditory canal ceruminous gland. They are subclassified as ceruminous adenocarcinomas, adenoid cystic carcinomas and mucoepidermoid carcinomas. Herein, we report a mucoepidermoid carcinoma case of external auditory canal.

Method: A 60-year-old male patient with a 1-year history of purulent discharge and bleeding in his left ear. He had a history of aural polyp excision and no malignancy was observed 2 years ago. Otoscopic examination revealed a polipoid mass arising from the left external auditory canal and the patient underwent an excisional biopsy.
Results: The histopathological examination revealed mucin-secreting and intermediate epithelial cells forming cribriform and solid nests. Tumour cells had minimal pleomorphism and mitotic figures. The patient was diagnosed as mucoepidermoid carcinoma.
Conclusion: The most common malignant tumour of the external auditory canal is squamous cell carcinoma. Ceruminous carcinomas are rare malignancies usually presenting with a polipoid mass in the outer ear canal of middle aged patients. Therefore, it can be challenging to diagnose for surgical pathologists and should be considered in the differential diagnosis.

E-PS-12-011
Epidermoid cyst in tongue: A case report
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Objective: Epidermoid cysts are benign lesions and they do not include structures such as hair follicles, sweat glands or sebaceous glands. They are often over and testicular in nature. %1 of epidermoid cysts are seen in the neck, especially oropharynx.
Method: 12-year-old girl admitted to the Plastic and Reconstructive Surgery clinic for painless swelling on the tongue. A soft asymptomatic mass with white yellowish color without evidence of trauma on the tongue was detected. The mass was excised and sent to pathology laboratory.
Results: Macroscopically, the material was cystic with a size of 5x3x3 cm.Cut surface had caseous material. On the microscopic examination, a cystic structure with intense keratin in the lumen and granular layer with pronounced stratifiye squamous epithelium was observed.
Conclusion: The epidermoid cyst is rare in the head and neck region. It is mostly seen in submental region of oral cavity. The appearance of the epidermoid cyst is extremely rare and very few cases have been reported in the literature. The differential diagnosis should be kept in mind because it is rare in this region.

E-PS-12-012
Localised amiloidosis in two patients; in tongue and vocal cords
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Objective: Amyloidosis; characterised with eosinophilic-amorphous depositions of fibrillar proteins, can be localised or systemic. Head and neck amyloidosis is rare. Herein, we report two-cases of AL-amyloidosis located in tongue and vocal-cords.
Method: Two men(34 and 71-year-old) applied with enlarged tongue and cough with dyspneic-periods lasting for about 2 weeks, respectively.The younger-patient had no medical history however the older - had hypertension and hyperlipidemia.Hematological-tests showed no cytopenias.Both cases had neither M-protein in serum-protein-electrophoresis nor Bence-Jones proteinuria.A mass of 2x1,5x1 cm on the tongue was observed in the older-patient.Endoscopic examination of the younger-patient revealed polypoid lesions in the right-vocal-cord and anterior-commissure.The patients underwent excisional biopsy.
Results: Microscopically both cases showed acellular, eosinophilic-amorphous depositions in the lamina propria of the vocal-cord and within the striated muscle of tongue.The deposits stained tile red with Kongo red stain and gave apple-green refle under polarized light.Systemic examinations, imaging-studies and bone-marrow biopsies were negative for myeloma and the cases were accepted as localised amyloidosis.
Conclusion: Amyloidosis can be divided into four categories:primary (plasma-cell-dyscrasias), secondary(systemic diseases such-as tuberculosis), hereditary (autosomal-dominant-inheritance) and localized-form.The localised form has the most excellent prognosis among all.The exclusion of primary and systemic reasons is the most important issue in dealing with amyloidosis because the most effective treatment is to control the primary disease.

E-PS-12-013
Osteomas of the tongue and the external ear: Two case reports
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Objective: Osseous lesions of the soft-tissues are rarely seen; however most of them can be seen in head-and-neck. Osteomas of the externa-ear and the tongue are uncommon benign tumours that need to be differentiated from malignancies. Clinical manifestations vary from no symptoms to recurrent local infections and external-ear cholesteatoma or a mass.
Method: Two women(28 and 35-year-old) applied with hard nodules on tongue and recurrent infections of external-ear, respectively. Both of the patients had no medical histories. A mass of 1 cm on the tongue and 0,8 cm in the external-ear were observed in the patients. Both of the lesions were totally excised.
Results: Microscopically both cases showed mature lamellar bone structures with bone-marrow inbetween just beneath the epithelium of the tongue and epidermis of the external-ear . However real osteoblastic and osteoclastic activity were not present. Some inflamation were present around the bone lamellae. Two lesions were diagnosed as Osteomas.
Conclusion: The origin of the osseous lesions in the head/neck are controversial. These lesions are firstly named as Osseous Choristoma and were accepted as congenital-malformation. When accompanying inflamation exists favouring a reactive/traumatic lesion with irregular borders and neoplastic ossification centers exist like Myositis ossificans; the lesion is named as osteoma.

E-PS-12-014
Osteosarcoma of the mandible: Report of three cases
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Objective: Osteosarcoma is a malignant neoplasm characterized by the formation of osteoid matrix by neoplastic cells. It commonly affects the long bones. The involvement of the mandible is rarely reported. Our aim is to review cases of mandibular osteosarcoma in order to study their clinical and pathological features.
Method: It was a retrospective study about 3 cases of mandibular osteosarcoma collected between 2006 and 2016 in the department of pathology at Salah Azaiez Institute of Tunis.
Results: The men age of patients was 53, 6 years. The sex ratio was 1/2. Functional symptoms were dominated mainly by swelling. Patients underwent a computed tomography san with identified a hyperdense lesion in two cases, hypodense lesion in one case. Microscopic examination showed chondroid differentiation in one case. The treatment was surgical in all patients. Complete tumour resection was performed on two patients. Recurrence occurred in all patients.
Conclusion: Mandibular osteosarcoma shows typical clinical behavior but varied radiological and histopathological features from those of its homologous in the long bones. Early diagnosis and prompt aggressive surgical intervention is the key for better prognosis.

E-PS-12-016

Sclerosing polycystic adenosis of parotid: A rare entity

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Objective: Sclerosing polycystic adenosis(SPA) is a rare inflammatory condition of the salivary glands characterized by fibrocystic changes and adenosis. Less than 60cases have been described in literature. We aim to report a case of SPA of the parotid gland with a brief review of literature.
Method: A 68-year old woman presented with a 4 months history of a painful mass of the parotid. On examination there was a well-defined, 1,5 cm mobile and firm mass of the right parotid. A fine needle aspiration biopsy specimen concluded to pleomorphic adenoma. Superficial parotidectomy was performed.
Results: On gross examination, the specimen measured 4 × 2x1cm and contained a 1 cm well-circumscribed unencapsulated nodule with inverted core. Intraoperative frozen-section concluded to benign lesions. Microscopic examination revealed a sharply circumscribed unencapsulated and lobulated nodule composed of acini, ducts and cribrifomr structures covered with round cells showing regular nuclei. Focally the cells exhibit large abundant eosinophilic cytoplasmic granules. The stroma was fibrous, hyalinized, harbouring an inflammatory infiltrate. Myxoid changes were observed. On immunohistochemistry, myoepithelial cells were detected using smooth-muscle-actin. At 3 months follow-up, the patient was free of local recurrence.
Conclusion: It remains unclear whether SPA of the salivary gland is an inflammatory pseudotumoural lesion or a neoplastic entity. Although, no carcinomatous degeneration has been reported yet, long-term follow up is advised.

E-PS-13 Molecular Pathology

E-PS-13-001

Morphometric characteristics of reparative, neoplastic and cancer spheroid epithelial-mesenchymal structure in cervical biopsy

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Objective: We evaluated the morphometric characteristics of reparative, neoplastic and cancer SEMS in biopsy with HPV associated uterine cervical cancerogenesis.
Method: Samples of 54 patients with uterine pathologies (15 chronic cervicitis, 12 L-SIL, 15 H-SIL and 12 carcinoma) were obtained and studied histological. Materials were fixed with 10 % formalin solution, parafinized then microtomed horizontally to thickness 4 μm. Parafinized histological samples were stained with H/E and studied immunohistochemically, with mAb against OCT4. Then measured area of different types of SB using the program cellSens Standard.
Results: OCT4 positivity appeared generally among SEMS. By sizes and histological characteristics, SEMS classified into three types: reparative, neoplastic and Cancer. The average area of reparative SEMS was 1141.1 ± 305.0 mkm2, the average area of neoplastic SEMS was 2553.9 ± 656.2 mkm2, the average area of cancer SEMS was 2553.9 ± 656.2 mkm2. Reparative SEMS distributed frequently among chronic cervicitis and L-SIL samples, while neoplastic SEMS showed significant positivity among the samples of L-SIL and H-SIL, cancer SEMS among carcinoma samples with distinguishable atypical polymorphic nucleus.
Conclusion: Different types of SEMS have their morphometric characteristicsas well as immunohistochemical and, which may be used for differential diagnosis of HPV associated uterine cervical pathologies.

E-PS-13-002

Estrogen and progesterone positive primary adenocarcinoma of the lung: A case report and review of the literature

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Objective: We report a case of primary adenocarcinoma of the lung with positive ER, PR expression (which can be observed in 4-11 % of all lung adenocarcinomas due to different authors).
Method: A 47-year old woman presented with tumour masses in proximal bronchus (4,5 cm), pleura and vertebrae. Biopsy from lung and pleura was performed.
Results: Microscopically in the lung and pleura there was tumour of similar histological pattern (adenocarcinoma). It was CK7, ER, PR positive, HER2 negative. Results of IHC study mislead the pathologist and the diagnosis was made in favor of breast carcinoma. Patient started to receive hormone therapy, but after thorough clinical examination a tumour mass in mammary gland was not found. Further investigation was made and tumour turned out to be TTF1 positive. Treatment was modified as for lung carcinoma and resulted in partial response (follow-up for 1,5 year).
Conclusion: ER,PR positive primary adenocarcinoma of lung can be a diagnostic challenge for pathologists. ER, PR positive tumour should be TTF negative thus to exclude lung origin. Probably, such tumours have better prognosis compared with ER,PR negative primary lung adenocarcinomas. Further investigation should be performed.

E-PS-13-004

Matrix-associated laser desorption/ionisation (MALDI) mass-spectrometry imaging in a study of IgA nephropathy linked to IgG4-sclerosing diseases

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Objective: IgG4-related kidney disease (IgG4-RKD) is an autoimmune systemic disorder characterized by dense infiltration of IgG4-positive plasma cells in kidneys, but can also manifest in multiple organs with their enlargement. IgG4-RKD often coexists with other glomerular diseases, such as mesangioproliferative glomerulonephritis or IgA-nephropathy (IgA-N), which is the most common primary glomerular disease worldwide. In addition, the course of the disease may be complicated by the presence of tubule-interstital nephritis (TIN). Proteomics and in particular Matrix-associated laser desorption/ionization (MALDI) mass-spectrometry imaging (MSI) has already been employed in the study of IgA-N by our group, detecting specific tissue markers. The aim of this study is to find specific overlapping proteins with IgG4-RKD, focusing on disease progression and possible application of the results in pathology.
Method: Kidney biopsies with confirmed diagnosis of IgA-N are analysed by MALDI-MSI. Immunohistochemical IgG4 staining, description of TIN, if present, and evaluation of increased IgG4 level in serum of these patients will also be performed.
Results: MSI data are currently under statistical elaboration and will be presented and discussed.

Conclusion: IgG4-RD is a recent entity often combined with other glomerulonephrites and TIN. The definition of molecular markers could play a crucial role in disease prognosis and predicting outcome.

E-PS-13-006

NGS in molecular pathology labs routine

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Objective: Next Generation Sequencing has revolutionized the detection of gene mutations due to its ability to screen multiple mutations in multiple genes simultaneously without the need to perform several sequential tests, overtaking the small biopsies barrier, in the continually raising of targeted therapy biomarkers, as well as cost effectiveness.
Method: DNA-extraction from formalin-fixed paraffin-embedded tumours were analyzed for NGS with a panel of 1825 hotspot mutations in 22 genes (Oncomine Solid Tumour DNA Kit) in Ion PGM. Mutations were detected using the Variant Caller plugin, the variant list was verified in the IGV and only mutations reported in the COSMIC database were reported.
Results: We studied 43 Lung Adenocarcinomas by NGS (Ion PGM); 37 cases had mutations, 24 of which presented more than one mutation. The driver mutations were: EGFR, KRAS, PIK3CA, ALK, ERBB2, BRAF, MET and SMAD4, as expected.
Conclusion: NGS has became more faster and requires less DNA for tests including more than two or three diferent genes, giving support to Molecular Pathology Labs as a robust method, prone to have simpler complements.

E-PS-13-007

Molecular cytogenetics in a case of paediatric rhabdomyosarcoma; proffering a better prognosis

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Objective: Rhabdomyosarcoma, a rare malignancy representing up to 50 % of sarcomas in paediatric patients is broadly categorised into two common morphological sub-types: embryonal and alveolar. Embryonal rhabdomyosarcoma survival rate is 90 % compared with alveolar (25 %), necessitating sub-typing. Morphology and immunohistochemistry profiles can overlap, therefore molecular cytogenetics is the best way of providing a definitive diagnosis. We aim to discuss the diagnostic work up of an orbital rhabdomyosarcoma focusing on the importance of molecular diagnostics.
Method: Review of a case including clinical details, histology, immunohistochemistry and molecular cytogenetics in combination with current literature.
Results: Fluorescent in situ hybridisation analysis showed no FOXO1 translocation typically found in alveolar rhabdomyosarcoma. Gains in chromosomes 2, 8, 11 and 12 were found in support of embryonal rhabdomyosarcoma.
Conclusion: Molecular and cytogenetic tests proved a vital part of the diagnostic process of this biopsy and led to a favourable tumour sub-type proffering a better prognosis.

E-PS-13-008

EGFR exon 20 p.T783A from cell-block - case report

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Objective: Somatic activating mutations in the TK domain of the EGFR confer tumour sensitivity to tyrosine kinase inhibitors (TKIs). Sensitive molecular testing strategies become the standard to determine targeted therapies in cancer patients management.
Method: DNA-extraction from formalin-fixed paraffin-embedded cell-block of ganglionar metastization with 50 % tumoural cells representation (66-years-old man with carcinoma - pulmonary/gastric/pancreatic origin) was analyzed for EGFR mutations by Next Generation Sequencing in Ion PGM (exons 18/19/20/21). Library preparation followed Oncomine Solid Tumour DNA Kit procedure. Results analysis was performed in Torrent Server and Ion Reporter as the Catalogue of Somatic Mutations in Cancer (COSMIC).
Results: EGFR exon 20 showed the mutation c.2347A>G;p.(Thr783Ala). This mutation confers tumour sensitivity to tyrosine kinase inhibitors (TKIs); EGFR exons 18, 19, and 21 and KRAS gene were wild-type.
Conclusion: This patient selection was crucial for treatment with EGFR TKIs. In the literature the c.2347A>G;p.(Thr783Ala) mutation was found in 1 % of EGFR mutations. The importance of sensitive molecular testing to detect novel EGFR gene mutations sensitive to TKIs, such as p.V765A, p.T783A, p.V774A, p.S784P, and p.V769A, are becoming standard. Ion PGM allows sequencing multiple hotspots within the same/ different genes in routine and this cell-block was representative.

E-PS-13-009

Optimal fixation conditions and DNA extraction methods for genotyping of FFPE tissue-derived DNA

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Objective: Tissue biopsies are routinely fixed in formaldehyde and preserved in paraffin blocks (formalin-fixed paraffin-embedded-FFPE) as this classical procedure preserves tissue structures for an accurate histopathological diagnosis. These samples are invaluable genetic resource for retrospective molecular genetic analysis. However, FFPE tissue samples are considered problematic starting material for most of the molecular genetic techniques due to the relatively low quality of extracted DNA.Therefore, our study is addresing the effects of tissue fixation procedures and DNA extraction methods of the DNA obtained for downstream analysis.
Method: Surgical specimens of colorectal cancer were fixed in 10 % buffered or nonbuffered formalin for 1, 12 to 24 hrs, or 48 to 60 hrs at 4oC or at room temperature (RT). DNA extracted from differently fixed and subsequently paraffin-embedded tissues was used for genotyping via PCR-RFLP technique. Three commercial DNA extraction kits were compared.
Results: Tissues fixed for 12 to 24 hrs in buffered formalin at 4oC temperature produced DNA with the most optimal quality for downstream analysis. These samples were successfully amplified with intense signal bands.
Conclusion: Conclusively, we have observed that in biomedical research using DNA from FFPE tissues it is important to control a few pretreatment steps: optimal pre fixation time, use of 10 % buffered formalin and use of cold temperature fixation (4oC) and absolutely avoiding of acidic pH environment.

E-PS-14 Other Topics

E-PS-14-001

Where do these guests come from? Diagnostic approach to metastatic lymph nodes

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Objective: In cases presented with lymphadenopathies without a primary focus found by simple radiological methods, the primary tumour can be diagnosed by histopathological evaluation of the metastatic lymph nodes. We aimed to discuss the nonhematological malignancies presented with lymphadenopathies and the histopathological results for primary tumours.
Method: In this retrospective study, cases diagnosed with metastasis in excisional lymph nodes between January 2013 and June 2016 were assessed for histopathological diagnostic approach and their relation with further clinical results.
Results: Among 832 lymph node biopsies, a total number of 21 cases, 12 male and 9 female, with a mean age of 57,23 (33–92) presented with nonhematological solid tumours were included. The most common localizations of the involved lymph nodes were inguinal (n = 8), axillary (n = 6), cervical (n = 4), and supraclavicular (n = 3) region. The most common primary tumours were malignant melanoma (n = 6), breast carcinoma (n = 4), ovarian carcinoma (n = 2), squamous cell carcinoma (n = 2), and germ cell tumour (n = 2). Others were papillary thyroid carcinoma, renal cell carcinoma, urothelial carcinoma, prostate adenocarcinoma and endometrial adenocarcinoma.
Conclusion: Nonhematological malignancies presented with lymphadenopathies are one of the most complicated occasions for clinicians. The histopathological evaluation of the excisional metastatic lymph node biopsies is an important method because of the cost effectiveness and easy applicability.

E-PS-14-003
Analysis, human resources reorganisation and quality management system implementation in an Anatomic Pathology Department
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Objective: Our Pathology department is composed by highly qualified personnel, distributed by areas of clinical and technical training, with some deficiencies in response times.
Method: The analysis of the current situation has been carried out, including strengths and weaknesses, always focused on optimization and deficiencies correction. In order to achieve this, indicators of productivity, labour safety standards, continuous training, and adequacy of personnel have been used. During 12 months, the redistribution of resources by areas of training, and the existing delays are analyzed. Training workshops are held, equipment is relocated and new modern communication channels are established.
Results: A Quality Commission group was reactivated involving phisician and lab technicians, interacting with the Hospital Main Quality Commission, in order to apply European regulations, Spanish society of pathology and prevention of occupational hazards recommendations.
Conclusion: We have achieved improvements in the staff qualification, participation of all personal in any service decision and basic training that favours completion of the tasks. Actually, there is still a shortage of pathologists and technical personal, although the involvement of all members admits raising expectations to achieve objectives. Our goal in the future is start up department accreditation towards norm UNE-EN ISO 15189.

E-PS-15 Pulmonary Pathology

E-PS-15-001
Bronchogenic cyst with an extremely rare lipoma-like appearance: Case report
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Objective: Bronchogenic cysts are congenital malformations, usually asymptomatic, resulting by abnormal development of the ventral foregut and lung budding during the first trimester. We present an extremely rare case of a lipoma-like bronchogenic cyst.
Method: A 38 years-old old man came in the Pneumology Department of Marius Nasta Hospital with irritative cough. Imagistic explorations revealed an anterior-superior mediastinal tumour. The surgeon removed a well demarcated mass that was molding the vasculare structures, without invasion. The tumour was sent to Pathology Department for further procedures and histopathological examination.
Results: The tumour (11/11,5/7 cm) had smooth external surface and a thin, transparent capsule. Cut surface was polymorph with fatty areas intricated with multiple cysts (yellowish-green gelatinous content) and pearlescent, glossy zones. The thickness of the cysts walls was 1–3 mm, with focal calcifications. Microscopy revealed matur adipous tissue, cystic areas, fibrocolagenotic tissue and calcifications. The inner surface of the cysts was lined by respiratory-type epithelium (pseudostratified columnar, ciliated) with submucosal glands, fascicles of smooth muscle and mature cartilage.
Conclusion: This bronchogenic cyst has an extremely rare lipoma-like appearance. We found only one similar case published in speciality literature. Other particularities are: multiple cysts, calcification (10 % of cases) and symptomatic presentation.

E-PS-15-002
Malignant pleural mesothelioma with no asbestos history: A case report
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Objective: Malignant pleural mesothelioma (MPM) is a rare and highly aggressive tumour arising from the mesothelial surface of the pleural space.This tumour was once rare, but its incidence rates are predicted to peak in the next few years.
Method: MPM is difficult to treat and commonly associated with asbestos exposure, which is its main risk factor.
Results: This cancer is a challenging diagnosis to make because of the insidious onset of symptomatology that leads to advanced stage and poor prognosis. The median survival rate is around 12 months. We present a case of a 59 year-old patient with no asbestos exposure who presented with left pleural hemorrhagic effusion and pleural thickening on CT scan.
Conclusion: Our pathology department confirmed the bleak diagnosis of diffuse epithelioid malignant mesothelioma, with pericardial and diaphragmatic invasion and lymph node metastasis.

E-PS-15-004
Combined small cell carcinoma: A report of a case and a potential pitfall
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Objective: Combined small cell lung carcinomas (CSCLCs) are small cell lung carcinomas (SCLCs) containing areas of non–small cell components (NSCLC), such as adenocarcinoma, squamous cell carcinoma, and large cell neuroendocrine carcinoma (LCNEC). We present a case of a patient diagnosed with a NSCLC on frozen sections and CSCLC on the resection specimen.
Method: A 63-year-old patient was referred to our hospital with a mass lesion of his right lower lobe and a tumour nodule of the upper right lobe. Intraoperatively, frozen sections were diagnostic of a NSCLC. He underwent a right low lobectomy and an upper lobe tumour resection.

Results: On dissection of the lobectomy specimen two neighbouring tumour foci of the hilum were found of 1,6 cm and 1,5 cm, with histological features of SCLC and adenocarcinoma respectively. The tumour nodule of the upper lobe was a NSCLC of the squamous or adenosquamous type.
Conclusion: The diagnosis of combined SCLC varies, depending on the tumour sample size, number of histological sections examined and type of specimen. An accurate recognition of CSCLCs is of great practical importance because treatment strategies are significantly different for SCLC and NSCLC. The inclusion of NSCLC component in frozen sections, in our case, resulted in surgical resection and final diagnosis.

E-PS-15-005
Pulmonary papillary adenoma: A case report and review of the literature
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Objective: Pulmonary papillary adenoma is a rare and benign tumour of the lung and until today less than 25 cases described in the literature. Although some cases shows infiltrative growth pattern it does not have metastasis or recurrence.
Method: The patient is a 38-year-old woman, who has diagnosed as undifferentiated nasopharyngeal carcinoma by nasopharyngeal punch biopsy in 2014. She was treated with concurrent radiotherapy and chemotherapy. In follow-up, multiple millimetric pulmonary nodules were detected on thorax computerized tomography 3 years after the initial diagnosis. The dominant nodule was 11 mm in diameter and had pathologic FDG uptake. The patient was operated to clarify whether the dominant nodule was primary or metastasis. The dominant nodule and two adjacent nodules were excised. Dominant nodule and one of the smaller ones were diagnosed as metastasis of nasopharyngeal carcinoma. The other nodule which is 6 mm in diameter was diagnosed as pulmonary papillary adenoma. The tumour is characterized by papillary structures lined by cuboidal epithelium. Neither mitosis nor atypia were detected and Ki-67 proliferation index was low.
Results: .
Conclusion: The clinicopathologic features and differential diagnosis of this rare neoplasm is presented with review of the literature and also this is the first case in Turkish literature.

E-PS-15-006
Neuroendocrine tumour of the lung with inusual stromal osseous metaplasia and bone marrow elements
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Objective: Pulmonary ossification is a rare phenomenon that can be considered exceptional when it includes bone marrow formation. We report a rare case of typical carcinoid with complete stromal bone metaplasia, where bone marrow elements are observed.
Method: Here we describe a 55-year-old man presenting with dyspnea. Subsequent chest computed tomography revealed a narrowing of the right superior lobe bronchus causing partial atelectasis of it.
Results: Surgical specimen showed a calcified lesion at the entrance of the right superior lobe bronchus which obstructed the bronchial lumen. The microscopic study revealed the presence of a typical carcinoid with complete stromal metaplasia with presence of bone marrow elements.
Conclusion: Typical carcinoid is a well-known primary endobronchial lung neoplasm accounting for 80–90 % of pulmonary carcinoid tumours. As many as 30 % of typical carcinoids may be accompanied by intralesional dystrophic calcifications, while complete ossification of these is an unusual finding scarcely reported in the literature. Ossification is more commonly associated with tumours of long duration. Extensive ossification is an unusual presentation for pulmonary carcinoid tumours, morover with bone marow elements. The implication of this phenotype remains elusive. Long-term follow-up of these patients is required to better characterize this phenomenon in disease progression.

E-PS-15-007
Resuscitation-related pulmonary bone marrow embolism: An accidental autopsy finding
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Objective: Pulmonary embolism, although frequently a clinically silent phenomenon, still causes a fairly stable incidence of sudden death. Fat and marrow embolism usually appears after long bone fractures. The aim of the report is to present a case of pulmonary bone marrow embolism after cardiopulmonary resuscitation.
Method: A 63-year-old female died unexpectedly with symptoms of cardio-respiratory failure after acute bleeding from duodenal ulcers. During recent years, she was repeatedly admitted to hospital because of upper gastrointestinal bleeding. An autopsy was performed.
Results: Autopsy disclosed multiple chronic duodenal ulcers in active and remission phases, as well as gastritis and duodenitis. Right-sided struvite-type kidney stones clinically correlated with severely decreased glomerular filtration rate and elevated creatinine level corresponding to chronic kidney disease. A component of acute kidney failure was noted. The gross fractures of two ribs and microscopical finding of pulmonary bone marrow embolism in small and medium-sized blood vessels were attributable to cardiopulmonary resuscitation.
Conclusion: Cardiopulmonary resuscitation-related rib fracture can cause pulmonary bone marrow embolism that has basically no importance as an autopsy finding. It may be considered a complication in patients with successful reanimation. Resuscitation-related pulmonary bone marrow embolism represents an important differential diagnosis to forensic traumatic death causes.

E-PS-15-008
Adenocarcinoma of lung associated with giant osteoclastic-like cells. A rare finding, histological study and electron microscopy
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Objective: Osteoclast-like giant cells (OLGCs) are extremely rare in lung carcinoma, generally are found within lesions that have a osteogenic component. There are only nine reported cases. We presented a case with clinicopathological and electron microscopy study.
Method: A 74-year-old man with 82-mm LID mass. An echobronchoscopy was performed with presence of multinucleated giant cells without evidence of epithelial cells. A lobectomy was performed.
Results: Morphologically , a giant osteoclast-like multinucleated giant cell tumour was observed with a stromal induced by mononuclear cells, lymphocytes, plasma cells together with an G3 adenocarcinoma. In the immunohistochemical study, expression for ck7 and TTF1 in the malignant epithelial component. The OLGCs showed positivity for vimentin, cd68, as well as mononuclear stromal cells. In the electron microscopy study, giant cell nuclei each surrounded by a nuclear envelope varie in shape from oval to those that were totaly irregular with deep maginal invaginations. Two mononuclear cell types, one has a round morphology and the second is spindle- shaped, fibroblast-like stromal cell.

Conclusion: Small biopsies or cytology study can cause diagnostic problems in terms of differential diagnosis. We believe these giant cell are part of a host response to the primary tumour, nowadays the biological significace of this reaction is unknow.

E-PS-15-009

Clinical case of adenosquamous lung carcinoma with EGFR mutation

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Objective: A 57-year –old woman, non-smoked, was admitted to clinic because of abnormal chest X-ray finding.
Method: The patient was performed surgery. By immunohistochemical method (IGH) two components were revealed in one lung tumour.
Results: 1) squamous cells cancer (SCC) which expressed cytokeratins (CK) 5/6 and didn't express p63 and TTF-1, napsin A. 2) adenocarcinoma and lymph nodes metastasis (3), creeping lapidary type, which cells expressed TTF-1, napsin A and didn't express CK5/6 and p63. Deletion was detected in 19 exon of gene EGFR in both components of the tumour. A month after the operation the patient complained on head subcutaneous metastasis - well-differentiated keratinizing SCC with the presence of horny pearls. IGH was carried out to identify mutations in the gene EGFR. Currently the patient receives treatment by Gefitinib.
Conclusion: Presented observation is of particular interest of that both components of the primary tumour and metastasis have EGFR gene mutation in the same deletion of 19 exon. Thus, these data indicate that we have described two-component tumour occurred, probably from poorly differentiated common precursor, which gave rise to two different populations of malignant cells.

E-PS-16 Soft Tissue and Bone Pathology

E-PS-16-001

Epidermal cyst of the sole

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Objective: Epidermal cyst (EC) arises mostly from the infundibular portion of the hair follicles.They appear every site of the body,especially on the face,scalp,neck and trunk.They originate rarely in areas without hair,such as the sole and palm.The ECs on the palms and soles are easily confused with warts or calluses.Obstruction of hair follicles and implantation of epidermal fragments into the dermis from a penetrating or blunt injury have been considered as causes of common ECs.
Method: A 31 year-old healthy woman presented with complaints of swelling on her right sole and pain during walking.The patient sustained sharp-pointed glass injury 2 years earlier.A soft tissue mass,firm,round,movable,1.8 cm in diameter and overlying the first web was detected by palpation on the plantar side of the right foot.Surgical excision was performed.
Results: A white cystic wall with white exudate was extirpated.Histopathological analysis revealed a stratified squamous epithelium structure similar to that of the skin and a clear granular layer.There were no signs of recurrence.
Conclusion: Although,the sole is an area without hair,EC should be in the list of differential diagnosis for plantar lesion of the foot.For proper treatment,careful dissection is a must to avoid the recurrence and the risk of damage to the underlying neurovascular structures.

E-PS-16-002

Inguinoscrotal angiomyofibroblastoma-like tumour: A case report

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Objective: Angiomyofibroblastoma-like(AMF-like) tumour is derivated from perivascular stem cells and has capacity of lipoid and myofibroblastic differentiation. This entity in male genitalia is exceedingly rare. Here we present a case of 49-years-old male patient who underwent left-sided inguinal hernia repair 3 years prior to admittance.
Method: The patient was admitted with pain and swelling in the lower left abdominal region, clinically suspicious for relapsing inguinal hernia. After medial laparotomy, tumourous formation together with the left testis was extirpated from inguinoscrotal region. A gross examination revelled solid relatively well demarcated pink-tan tumour measuring 9,5x6x5,5 cm, including the vas deferens from the spermatic cord, without involvement of testis and epididymis. Standard procedure for histology and immunohistochemistry was made.
Results: Microscopically the tumour was composed of spindle-shaped cells and small vessels proliferating in edematous and focally fibroblastic stroma admixed with mature adipocytes. The tumour was positive for SMA, Vimentin and CD34, with focal Desmin expression, low proliferation index Ki-67(<1 %) and negative for S-100, HMB45 and PR. Pathological diagnosis for AMF-like tumour was made.
Conclusion: AMF-like tumours are rare and potentially recurrent mesenchymal neoplasms with lack of information regarding its characteristics. Therefore long-term follow-up is necessary and essential for appropriate patient care.

E-PS-16-003

Epithelioid inflammatory myofibroblastic sarcoma: A case report

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Objective: Inflammatory myofibroblastic tumour (IMT) is a mesenchymal neoplasm of intermediate biological potential. We aim to report a case of Epithelioid inflammatory myofibroblastic sarcoma (EIMS), a rare variant of IMT with predilection for male patients, distinctive morphological, immunohistochemical and genetic features and malignant behavior.
Method: Six month-old boy, with abdominal swelling, performed an ultrasound that showed a 11x9cm well-defined hepatic mass, suggesting hepatoblastoma. CT-scan displayed a large intra-abdominal neoplasm (10x11x8cm) without infiltration of adjacent organs. A biopsy was performed and a diagnosis of IMT was rendered. He underwent surgical excision of the mass and multiple peritoneal implants.
Results: Microscopically, the neoplasm was composed of spindle/round cells with vesicular nuclei, prominent nucleoli and scanty cytoplasm, admixed with polymorphic inflammatory infiltrate. Immunoexpression for desmin and ALK (cytoplasmic, with perinuclear accentuation) was observed. FISH showed rearrangement of ALK; karyotype demonstrated an inversion of chromosome 2, involving ALK e RANBP2 genes. A final diagnosis of EIMS was made. The patient underwent chemotherapy (Euro-Ewing protocol). Three years after diagnosis he is alive without evidence of disease.
Conclusion: EIMS is a rare and highly aggressive variant of IMT. Pathologists must be aware of its distinctive features because an accurate diagnosis is vital for the correct management of these patients.

E-PS-16-004

Pleomorphic cell lipoma: A scary morphology for a gentle tumour. A case report

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Objective: Pleomorphic lipoma is a relatively rare adipocytic neoplasm, occurring predominantly in elderly males in the subcutaneous tissues of the neck or shoulder. The objective of our work and through this observation to highlight this entity frequently leads to misdiagnosis as liposarcoma, because of confused histology and the pleomorphism of the lesion. Criteria for the differentiation from the various types of liposarcoma are discussed.
Method: We report the case of a patient, 50 years old, who presented for Pendulum mass at arm level, Which was superficial, mobile and painless
Results: The macroscopic examination showed an encapsulated mass measuring 13X7X6 cm, with a plane of cleavage with respect to the skin, it is of fibro-greasy appearance with myxoid zones. The microscopic examination showed the presence of a mature adipocytic contingent, separated by large fibrous septa, the seat of many atypical cells with monstrous nuclei, sometimes giving a rosette appearance, it is also seen lipoblast like cells, which posed the problem of differential diagnosis with liposarcoma, CD34 staining by immunohistochemistry further supported the diagnosis.
Conclusion: Pleomorphic lipomas are "clinicopathologic" entities, which necessitate attention to details such as the age and sex of the patient, the anatomic plane of the tumour, and this particular giant cell-rich morphology

E-PS-16-005

Agressive osteosarcoma with unusual presentation and evolution

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Objective: Osteosarcoma is the second most common malignant tumour of the bones. Nevertheless, the distal upper extremities are an extremely rare localisation, accounting for only 0.18 % of all osteosarcomas. Multiagent chemotherapy in combination with wide excision is a highly effective treatment for this neoplasm.
Method: We present a 15 year old patient with a distal ulnar mass on imaging, suspicious for either Ewing sarcoma or Osteosarcoma. He was diagnosed with Osteosarcoma on a biopsy. An increase in tumour mass was detected radiologically after several cycles of neoadyuvant chemotherapy. Thus, an amputation was performed.
Results: We confirm the diagnosis of osteogenic sarcoma with areas of osteoblastic and chondroblastic differentiation upon histological examination of the surgical specimen. The patient receives adyuvant chemotherapy and is disease-free 7 months afterwards.
Conclusion: We consider the combination of localisation, response to therapy and outcome to be quite noteworthy for this type of tumour.

E-PS-16-007

Extraskeletal myxoid chondrosarcoma metastasis to the lung: A case report

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Objective: Extraskeletal myxoid chondrosarcoma (EMC) is a rare mesenchymal tumour. This sarcoma usually presents as a slow growing, palpable mass in the extremities. Here, we report a very unique case of extraskeletal myxoid chondrosarcoma that metastasized to the lung 8 years after the first diagnosis.
Method: A 67-year-old female patient with a history of EMC of the right thigh presented to the emergency department complaining of chest pain and coughing. A PET/CT scan showed a hypermetabolic solid mass with lobulated borders that was located in the right inferior lobe. A wedge resection was performed.
Results: The microscopical examination showed a neoplasm that was constituted of cords of small cells with small round nuclei and eosinophilic cytoplasm immerse in an abundant myxoid matrix. The immunohistochemistry showed positivity for vimentin and negativity for S-100 protein and cytokeratin AE1-AE3. Ki-67 proliferation index was 1 %. The final pathology report revealed a metastatic extraskeletal myxoid chondrosarcoma.
Conclusion: MC is an intermediate-grade neoplasm characterized by a long clinical course with high potential for distant metastasis. Being able to make the correct diagnosis relies on morphologic examination and immunohistochemistry. Molecular pathology is helpful when necessary.

E-PS-16-008

Lipomatous tumours: Challenges in daily practice

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Objective: Lipomatous tumours are one of the most complex areas of soft tissue pathology. The different subtypes vary greatly with regard to site of involvement, morphologic appearance, and behavior. We summarized the problems and controversies in diagnosis of adipocytic tumours in daily practice.
Method: A series of 35 patients with lipomatous tumours diagnosed in 2014–2016, at Theageneion Cancer Hospital was studied. Tissue samples were stained with H&E to determine the histopathological type of patients' tumours, mainly based on morphological features and correlated with patients' age, gender and site of involvement.
Results: Five different histological subtypes were revealed, comprising of angiolipoma (37,1 %), atypical lipomatous tumour/well-differentiated liposarcoma (28,5 %), spindle cell lipoma/ pleomorphic lipoma (20 %), intramuscular lipoma (11,4 %), and angiomyolipoma (2,8 %). The average age was 56,7 years (range: 31–82). Males are affected predominantly by spindle cell lipoma, while females by intramuscular lipoma. Extremities are the most common location for angiolipoma, and shoulder and neck for spindle cell lipoma.
Conclusion: The differential diagnosis mainly is based on morphological criteria and the available immunohistochemical stains are less useful. Of particular diagnostic importance has been the recognition of spindle cell/pleomorphic lipoma, frequently misdiagnosed as liposarcoma or other sarcoma types.

E-PS-16-009

Classic adamantioma: A case report

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Objective: Adamantinoma is a rare primary bone tumour presenting in patients with a median age of 25–35 years, slightly predominant in males, commonly found in the anterior metaphysis or diaphysis of the tibia in 85–90 % of cases.
Method: A 14-year-old female patient, without medical history, presented with gradually increasing swelling of the right leg in the last 3 years. Radiology revealed an eccentric lesion, occupying the anterior cortical of the right tíbia.

Results: Patient underwent biopsy that suggested Adamantinoma. Surgical excision was performed, consisting of a segment of the tibia with 6 cm. Cut sections revealed eccentric lesion with whitish, homogenous and elastic tissue, involving the soft tissue in a width of 0,8 cm. Histopathologically showed clusters of epithelial cells with peripheral palisading in a fibrous stroma with haphazard osteoid deposition, without squamous differentiation. Surgical margins were negative. Immunohistochemistry revealed positivity for AE1/AE3, p63, CK5/6 and vimentin. Morphological and immunohistochemical results are diagnostic of Classic Adamantinoma.
Conclusion: Adamantinomas metastasize in 12–29 % of patients with comparable mortality rates. Recurrence risk factors are intralesional/marginal surgery, extra compartmental growth, lack of squamous differentiation of the tumour, increased epithelium-to-stroma ratio, young females, and pain at presentation. After 3 months of follow-up, the patient is well, without pain or tumour relapse.

E-PS-16-010
Infantile Myofibromatosis: A clinicopathological study of 3 cases
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Objective: Infantile Myofibromatosis (IMF) is a rare mesenchymal tumour of infancy and early childhood . Three clinical forms were described the solitary form and multicentric form with or without visceral involvement. Our objective is to determine the epidemiological, clinicopathological characteristics and outcome of Infantile Myofibromatosis.
Method: It is a retrospective study of 3 cases of IMF collected from our department over a 12-year-period.
Results: The first case was male new born who was seen on day 3 of life with neonatal bowel obstruction. An abdominal ultrasound revealed a large ileal mass . The second patient was a female that presented at birth multiple subcutaneous nodules involving the neck,the trunk and extremities . The last case was a 13 year old boy who is followed for parietal basithoracic tumour with four recidivism and visceral involvement (duodenum, pancreas). Histological exams revealed a proliferation of ovoid or spindle cells arranged in short fascicule with a central hemangiopericytoma-like vascular pattern .
Conclusion: Infantile Myofibromatosis is the most common fibrous tumour in infancy and should be considered in any infant with multiple subcutaneous nodules.Treatment and prognosis depend on its location and form of presentation.

E-PS-16-011
Angiomatoid fibrous histiocytoma: Atypical site and symptoms, a diagnostic challenge, about a case
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Objective: Angiomatoid fibrous histiocytoma (AHF) is a rare tumour with intermediate malignancy potential, intramuscular location is very uncomun. The objective of our workto highlight this entity often under diagnosed, because of confused imagery, a deceptive histology and especially the lack , in our country, of diagnostic means that makes use of the FISH for diagnostic purposes an exception.
Method: We report the case of a young adult patient, 29 years old, who presented for abdominal pain with dorsal irradiation with normal clinical examination, MRI has objectified a posterior intercostal lesional process, in intra muscular.
Results: A first biopsy was done, we had a indeferenciated proliferation mimicking metastatic carcinoma, it was positive for CD68, and EMA, negative for Desmin and auther markers, we proposed AHF and confirmation is made after resection, with typical morphology. we have no means to make FICH commonly in our country.
Conclusion: The problem which arises is to be able to eliminate the other differential diagnoses, and which can lead to heavy treatments, these are dominated by angiosarcoma, rhabdomyosarcoma, Kaposi's disease and ganglion metastases. Although rare, an AHF should be evoked in front of a slowly evolving tumour with systemic manifestations. A precise preoperative diagnosis allows a price in adequate therapeutic load by avoiding mutilating surgery.

E-PS-16-012
Fibrosarcomatous variant of dermatofibrosarcoma protuberans: Clinicopathologic analysis of 3 cases
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Objective: Infantile Myofibromatosis (IMF) is a rare mesenchymal tumour of infancy and early childhood . Three clinical forms were described the solitary form and multicentric form with or without visceral involvement. Our objective is to determine the epidemiological, clinicopathological characteristics and outcome of Infantile Myofibromatosis.
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Conclusion: Infantile Myofibromatosis is the most common fibrous tumour in infancy and should be considered in any infant with multiple subcutaneous nodules.Treatment and prognosis depend on its location and form of presentation.

E-PS-16-013
Soft tissue malignant PEComas: Revision of two cases
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Objective: The term perivascular epithelioid cell tumour has been applied to a family of tumours composed of perivascular epithelioid cells. Our objective is to revise the cases of soft tissues malignant PEComas diagnosed in our department analysing histology, immunohistochemistry, and prognosis.
Method: We found two cases of soft tissues malignant PEComas in our archives.
Results: The first case was received in 2015, as a left thigh tumourectomy of a 39 year old female with a diameter of 9 cm and the second case was received in 2016, as a right thigh tumourectomy with a diameter of 11 cm. In both cases, We identified a soft tissue tumour with perivascular epithelioid cells that were positive for HMB45, Melan A and TFE3 surronded by necrotic areas. Both had features of malignancy: they were greater than 5 cm and microscopically had more than 1 mytosis/50 HPF, high nuclear rate, and large necrotic areas. The first patient, died 1 year later because of her disease and the other is free of disease at the moment.

Conclusion: Soft tissue PEComas are rare tumours with a characteristic pattern with perivascular epithelioid cells which stain with melanocytic markers. Malignancy features (necrosis, mytosis, vascular invasion) are important to notice, because they can predict a worse prognosis.

E-PS-16-016

Benign-looking primary fibrosarcoma of the uterus

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Objective: We present a case of a young woman with a primary uterine fibrosarcoma with features of an epithelioid sclerosing fibrosarcoma, primary diagnosed as a leiomyoma.
Method: The complex differential diagnosis involved radiological and pathological analyses with utilization of immunohistochemical and molecular methods.
Results: In 2013, a 38 years-old woman with myomatous uterus underwent a subtotal hysterectomy. The tumour was diagnosed as a sclerosing leiomyoma. In 2015, the woman presented with multiple metastases in the abdomen. The histopathological view was consistent among primary uterine and metastatic tumours. The neoplasm was composed of fibrotic tissue with foci of sclerosis and collagen formation. The well-differentiated tumour cells had epithelioid look. Mitoses were scarce. The tumours were positive for: MUC4, vimentin and Masson-trichrom histochemical stain. The neoplasm was negative for: CD56, calretinin, inhibin, SMA, desmin, h-caldesmon, CD117, ER, PR, CD10, CD34, S100p, HMB-45, CKAE1/AE3. Ki67 index was up to 5 %. All features vouched strongly against the diagnosis of leiomyosarcoma, endometrial stromal sarcoma or sex cord tumour and the final diagnosis was a primary uterine sarcoma with features of a sclerosing epithelioid fibrosarcoma.
Conclusion: We decided to report on the case, because of the tumour's unique presentation and its similarity to a benign sclerosing leiomyoma.

E-PS-16-017

Extrapleural solitary fibrous tumour: Clinicopathological and immunohistochemical analysis of 19 cases

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Objective: Extra-pleural Solitary Fibrous Tumour (SFT) is a rare tumour that it's clinical, pathological and immunohistochemical features overlap with hemangiopericytoma and creates differential diagnosis problems because of its histological variety.
Method: The clinical, pathological and immunohistochemical features of the cases which diagnosed SFT or hemangiopericytoma in our department between 2007 and 2016 have been re-examined.
Results: The mean age was 56 (range 19–86) and 55 % were male. The mean tumour size was 6.3 cm (range 0.4–13.5 cm). SFT arose at different anatomical sites; including abdominal, nasal cavity, paratesticular, prostate and extremites. In our 19 cases 6(31 %) were malignant. Histologically; tumoural infiltration which has fibrous- hyalinised stroma, which consist of cells, round-oval nucleus, indistinct cytoplasmic borders was detected. Many thin walled ectatic vessels were found interspersed within the tumour cells and resembled hemagiopericytoma-like. There were marked cytological atypia, mitosis, necrosis in malign cases, not in benign ones. Immunohistochemically, CD99 and bcl-2 was positive in 16 and 15 cases respectively; CD34 was positive in all cases.
Conclusion: SFT is a tumour that should be kept in mind because it can be seen outside the pleura and shows different patterns.

E-PS-16-018

Tumoural calcium pyrophosphate dehydrate crystal deposition disease of temporomandibular joint: A pitfall in the diagnosis of chondrosarcoma

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Objective: Tumoural calcium pyrophosphate dehydrate crystal deposition disease / tumoural or tophaceous pseudogout is a rare, benign entity that mimics skeletal malignancy particularly chondrosarcoma
Method: We report a case of a 80 year-old male presented with a quite large, tumour- like lesion of the right temporomandibular joint. According to CT findings and FNA cytology report, the diagnosis of a chondrosarcoma was initially made. An incisional biopsy was performed
Results: Histological examination showed a lesion mainly composed of basophilic calcified material, histiocytes and foreign body giant cells. Rhomboid / needle-shaped crystals, weakly birefringent on polarized microscopy were identified. Chondroid metaplasia was also present. Neither necrosis nor mitoses were found
Conclusion: The diagnosis of tumoural calcium pyrophosphate dehydrate crystal deposition disease / tumoural or tophaceous pseudogout by simple, morphological criteria is extremely important and crucial. The danger of misdiagnosing a cartilaginous tumour, especially chondrosarcoma, should be avoided, as it requires different and more aggressive therapeutic approach

E-PS-16-019

Unrecognised alkaptonuria and ochronosis: A rare cause of severe arthropathy

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Objective: Alkaptonuria is a rare metabolic disorder characterized by a deficiency of the homogentisic acid oxidase enzyme. The result is accumulation of homogentisic acid throughout the body, which leads to gradual development of a phenomenon known as ochronosis, characterised by urine darkening, progressive scleral, subcutaneous and cartilage pigmentation and degenerative ochronotic arthropathy.
Method: We present a case of a 57 years-old female who was admitted to the Orthopedics and Traumatology Department of the Emergency County Hospital Miercurea Ciuc with functional impotence of the right hip, vicious position of the leg and groin pain exacerbated by passive movements.
Results: On the CT scan a Garden 3 right femoral fracture was described associated with degenerative lesions of the lumbar spine, generalized osteopenia and bilateral ilioischial osteoclerotic lesions. A total cemented right hip arthroplasty was performed. Intraoperatively a dark discoloration of the joint has been found and a histopathological examination was requested from the right femoral head and from the capsulo-ligamentar fragments. The microscopic examination revealed bone fragments with degenerative changes coverd on the surface by brown cartilage and sharp, irregular, brown cartilage fragments embedded in the capsulo-ligamentar soft tissues. The diagnosis of ochronotic artropathy was made and a clinical reassesment and the determination of the serum level of the homogentisic acid was suggested, which confirmed the diagnosis.
Conclusion: Ochronotic arthropathy is often diagnosed during a total joint replacement and may not be suspected until dark synovium and cartilaginous surfaces are found intraoperatively.

E-PS-16-020

Atypical spindle cell lipomas: Histological and immunhistochemical analysis of 11 cases

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Objective: The term of atypical spindle cell lipomas is identified, the lesions which have distinct component of spindle cells, conspicious atypia, low grade appereance and the same immunhistochemical signs with the spindle cell lipomas, in recent years. However there is noconcensus or identification and nomaclature.
Method: Eleven cases of atypical spindle cell lipomas showing atypical histhologic features were identified in our department in 2009–2016. We reexamined the clinical, histologycal and immünohistochemical features of this cases.
Results: The mean age was 65,4, the mean diameter was 3,9 cm and 9 % of cases were female. Localisation of tumours are: back, nape, scalp, leg, shoulder and cheek. All cases had ropey-like collagen and mixoid backround were present in 5 cases. Additionally 5 cases were encapsulated, pleomorphic cells were present in 2, psödoangiomatous patern was present in 1, hemangiopericytoma-like vasculer patern were pesent in 1 case. Mast cells were considerably remarkable in all cases. Immunohistochemical features: CD 34 (+) in all, S-100 focal and weakly (+) in 2, desmin weakly (+) in 3, Rb (-) in 9, MDM-2 (-) in all cases.
Conclusion: Presence of spindle cells in lipomatous tumours cause diagnostic difficulty with liposarcomas. Therefore, if it is possible clinical, histological, immunohistochemical and molecular examination should be done detailed.

E-PS-16-021

Giant cell angiofibroma. Report of a case

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Objective: We present a case of a giant cell angiofibroma(GCA) and discuss the differential diagnosis.
Method: A 29-year old female patient was admitted in the outpatient clinic of the ophthalmology department with a history of slow growing painful mass of the left eyelid measuring 2.2x1.8x1.6 cm. Excision of the tumour was performed.
Results: On microscopic examination the tumour was unencapsulated, characterised by a patternless spindle-shaped cell proliferation, a prominent network of small blood vessels and scaterred multinucleated giant cells, with some of the nuclei forming a floret pattern. Mitotic count was low (1–2 mitoses/10 HPF). Immunohistochemically the tumour cells were positive for Vimentin, CD-34, CD-99 while S-100, CD-31, CD-117, FLI-1, factor VIII, BCL-2 and CD-68 were negative. The differential diagnosis included mainly GCA, giant cell fibroblastoma, solitary fibrous tumour and a benign vascular tumour. Giant cell fibroblastoma and solitary fibrous tumour were excluded since the first is infiltrative and occurs in early childhood and the second lacks giant cells.
Conclusion: The tumour was diagnosed as consistent with GCA. The patient showed no evidence of recurrence with 16 months of follow-up.

E-PS-16-023

Calcifying fibrous tumour of small bowel causing intussusception

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Objective: Calcifying fibrous tumour is a rare benign lesion with a broad differential diagnosis. The aim of this case report is to raise awareness regarding this unusual entity and its clinical implications.
Method: A 54 year-old woman presented to the Emergency Department with abdominal pain. Exploratory laparotomy revealed an intramural small intestinal tumour causing intussusception.
Results: Grossly, the tumour was well-circumscribed, non-encapsulated, with tan-white cut surface, and measured 2.1 cm. Microscopically, the lesion was composed of scattered, bland, spindle cells arranged in bundles within hyalinized collagenous stroma. No cellular atypia or mitotic activity was present. On immunohistochemical stains, these neoplastic cells expressed vimentin, and were negative for smooth muscle actin, desmin, caldesmon, β-catenin, ALK-1, CD117, CD34 and S-100 protein. Histochemical stains (Congo red and Verhoeff–Van Gieson) did not reveal amyloid or degenerated elastic fibers. Foci of dystrophic and psammomatous calcifications, as well as inflammatory cell aggregates composed of lymphocytes, plasma cells and eosinophils were present.
Conclusion: Calcifying fibrous tumour is a benign lesion, which can be observed in any location, and may have significant clinical implications, such as intussusception. Immunohistochemical stains are useful in ruling out other conditions with similar histologic findings.

E-PS-16-024

Mesenteric cystic lymphangioma: A case report

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Objective: Cystic lymphangiomas (CL) are rare benign tumours. They are preferentially located in the head, neck and axilla in children. However, lymphangiomas in the peritoneal cavity are extremely rare, particularly in adults. In the abdomen, lymphangiomas occur most commonly in the mesentery, followed by the omentum, mesocolon and retroperitoneum. Most reports show female predominance.
Method: A 46-year-old male patient presented complaining of a painfull abdominal mass. The cystic mass was 22 cm in diameter and it was removed.
Results: The histopathological examination of the resected specimen was consistent with typical findings of a CL: dilated lymphatic vessels, lined with flattened endothelial cells without atypia, and with abundant lymphoid tissue. In addition, smooth muscle cells and foam cells containing lipid material were reflected in the wall.
Conclusion: Diagnosis of intra-abdominal CL is difficult because of its rarity. The intra-abdominal lymphangiomas are essentially located in the mesentery, but may relate to the gastrointestinal tract, spleen, liver, kidneys, adrenals and pancreas. Retroperitoneal location appears to be rare. We are presenting this case because of its rare localisation.

E-PS-16-025

Primary neoplasm of the liver with perivascular epitheliod-cell differentiation (PEComa): A case report

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Objective: Neoplasms with perivascular epitheliod-cell differentiation (PEComas) are rare mesenchymal tumours, characterized by perivascular cell arrangement and melanocytic/muscular differentiation. They can arise in different anatomic locations but hepatic PEComas are exceedingly rare.
Method: A 46-year-old man presented with an atypical abdominal pain for the last few months. Clinical examination revealed a palpable liver

mass. Laboratory examination, including tumour markers, was normal. CT scan showed a heterogeneously enhanced mass, located between the I and IV segments. The patient had no history of cirrhosis or hepatitis. A left hepatectomy was performed.
Results: Gross examination revealed a soft lesion measured 8.4X7.3X4.7 cm, with rather demarcated margins and whitish in color. Histologically, the tumour was composed of nests and sheets of large epitheliod cells with abundant eosinophilic/pale cytoplasm, round nuclei and rare mitoses. A sinusoidal vascular network and radial cell arrangement around blood vessels were apparent. Necrosis or other tissue elements were not identified. Immunohistochemically, the cells exhibited expression only for vimentin, HMB45, Melan-A and SMA. A diagnosis of PEComa of uncertain malignant potential (Folpe's criteria) was made.
Conclusion: Hepatic PEComas are very rare neoplasms and, to our knowledge, ~20 cases have been reported in the literature. The tumour is histologically diagnosed, since the clinical/imaging findings are atypical.

E-PS-16-026
Ewing sarcoma: Unusual presentation in an unusual patient
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Objective: We present the case of a 62 y/o male that came to our attention after a three-month history of back pain, that debuted with neurological focality.
Method: Lumbosacral MRI revealed large enchancing mass, occupying the body and posterior arch of the T11 vertebra with paravertebral soft tisuue extension.
Results: The lesion was successfully resected. The histopathological examination revealed a densely-cellular "blue tumour", composed of small round cells uniformly arranged in sheets. Neoplastic cells had scant cytoplasm and round nuclei with finely dispersed chromatin, being diffusely immunopositive for CD99. FISH analysis confirmed the presence of an EWS-FLI-1 translocation (11;22). The morphological and immunohistochemical profile was indicative of Ewing's sarcoma.
Conclusion: Ewing's sarcoma is most frecuently seen in children, mostly arising in patients under 20 years of age. This tumour rarely originates in the spine, and even more rarely there, if the sacrum is excluded. This is the reason why there are still concerns about the optimal treatment, especially in adults, as is our case.

E-PS-16-028
A rare case of severe degenerative knee joint disease due to torture in a refugee from Sudan to Greece
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Objective: A case of severe degenerative joint disease following bilateral total knee dislocation due to torture in a refugee who arrived in Greece from Sudan and to highlight the impact of refugee crisis in public health systems.
Method: A 35 year old male presented at the emergency room with painful limps, using two walking sticks as walking aids. The history revealed that the patient was a victim of torture in Sudan, who sought refuge in Greece. The knees were edematous and radiography revealed complete dislocation of the knee joints. On histological examination, the signs of severe degenerative joint disease were all present; fissures and clefts at the articular cartilage, duplication of the tidemark, cyst formation and severe thickening of the synovial bursae.
Results: Knee dislocation usually happens on a background of acute injury. In our case it was the sustained torture which caused the dislocation of the knees and, subsequently, the severe degenerative joint disease. Notably, despite the financial crisis in Greece, all the refugees are treated free of charge in public hospitals, a fact completely reasonable in terms of humanity. This seems to be well recognized by the European Union which accepts thousands of refugees over the last years and finances supporting programs.
Conclusion: The recent movement of refugees in Greece, from countries at war and poor living conditions make doctors face up with diseases or causes of diseases which are mostly unknown and only historically described in the medical textbooks.

E-PS-16-030
Angiomatoid fibrous histiocytoma
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Objective: Angiomatoid fibrous histiocytoma, formerly classified as malignant, is a soft tissue tumour characterized by specific chromosomal alterations the most common being t(2;22)(q33;q12) and t(12;22)(q33;q12) which are also found in clear cell sarcoma .Clinical impression is usually of a benign tumour or cyst .Excision with clear margins is the treatment of choice.
Method: We herewith report two cases.: a 15-year-old female with a tumour located in her right arm and 13-year-old male with a tumour located in the middle finger of his left hand. Both tumours were circumscribed with a solid cut surface and patchy blood-filled cystic spaces.
Results: Characteristic histology of angiomatoid fibrous histiocytoma was observed: a fibrous pseudocapsule, a round to oval or spindle cell proliferation, a pseudoangiomatous pattern and a lymphocytic cuff. Both tumours were positive for desmin , EMA, CD68 and CD99 whereas ALK was negative. Neither has experienced recurrence after five and 1 year respectively.
Conclusion: Angiomatoid fibrous histiocytoma is a tumour of intermediate malignancy therefore, correct diagnosis is mandatory. Recurrence is unusual and seems to be associated with infiltrative borders and deep location but not with mitotic activity. Metastatic cases have been reported.

E-PS-16-031
Paediatric malignant perivascular epitheloid cell tumour with unusual immunophenotype
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Objective: Perivascular epitheloid cell tumour (PEComa) represents a rare group of mesenchymal neoplasms characterized by the presence of epitheloid cells of mixed myo-melanocytic differentiation with unpredictable malignant potential expressing myogenic and melanocytic markers. We present a case of malignant PEComa of soft tissue in a 10-year old girl with peculiar melanocytic tumour cells "immunophenotype" negative for HMB-45 and Melan, but positive for MITF.
Method: A 10-year-old girl presented with a 3-week history of slowly progressive painless, well circumscribed swelling, measuring 3 cm in diameter, under her left clavicle. The ultrasound showed well defined, echogenic heterogeneous soft tissue mass with discrete vascularization. Fine needle aspiration was suspicious for malignant mesenchymal tumour therefore complete resection was done.
Results: Macroscopically, the mass was whitish and lobular while microscopic findings confirmed diagnosis of PEComa. Two weeks after the surgery, at the site of the primary tumour, the painless nodules were palpable, measuring 5 and 10 mm in diameter respectively. Re-excision

was performed, showing a tumour with the same morphology as earlier lesion.
Conclusion: Tumours of this type are often associated with an aggressive clinical course although the majority of PEComas exhibit benign or indolent behavior. To the best of our knowledge, this is the first reported case of malignant PEComa in such young patient.

E-PS-17 Thymic and Mediastinal Pathology

E-PS-17-001
Tumours of the thymus: Review of cases in Cruces Universitary Hospital over the last 5 years

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Objective: The aim of this study is to classify the cases of thymic epithelial neoplasms, on the basis of the histological classification accepted (Masaoka stage and WHO types)
Method: Retrospective study of the medical records and archival tissue sections of all cases with a diagnosis of thymoma in Cruces University Hospital between 2012 and 2017
Results: We found 18 cases, with a mean age of 55.9 years (range 38–64). A slight female predominance was noted (11 cases, 61.1 %). On average, type B2 was the most frequent tumour, accounting for 27.7 % of thymomas (5 cases). It is important to notice that we described 3 mixed/combined neoplasms, which consisted of type B3 and B2 components. Despite the fact that nearly all the specimens were encapsulated, 8 cases (44.4 %) showed invasion of the adjacent mediastinal fat (stage II)
Conclusion: Thymoma is a rare malignancy overall, but it is the most common mediastinal tumour in adults. No environmental, viral or nutritional factors appear to play an etiological role in these neoplasms. They are more common in middle-aged adults, and mostly found in stage I (noninvasive). All histological types have the capability to invade, recurred and metastasize. Increased survival is closely associated with completeness of excision.

E-PS-18 Uropathology

E-PS-18-001
Morphological and immunohistochemical features of cystic renal tumours in adults

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Objective: Predominantly cystic renal neoplasm have been the source of diagnostic confusion and controversy. Recently epidemiological data suggest an increasing incidence of these tumours. The aim of this study was to evaluate the pathological and immunohistochemical features of cystic renal tumours.
Method: A retrospective study was performed in order to identify patients with cystic renal tumours in a period of 10 years. We analyzed the clinicopathological characteristics and immunohistochemical profile of these tumours.
Results: We identified 11 cases of cystic renal tumours: 4 cystic nephromas(CN), 5 multilocular cystic renal cell carcinoma(MCRCC),1 cystic renal cell carcinoma and 1 cystic synovial sarcoma. CN involved the left kidney of 4 women with mean age 56 years. 5 patients have unilateral MCRCC with left predominance, 3 were male and 2 female. Sixty-six percent of MCRCC were confined to the kidney (pT1); half of them were associated with other renal lesions including renomedullary interstitial cell tumour and angiomyolipoma.
Conclusion: The recognition of MCRCC and CN is very important because patients may benefit from conservative surgery (nephron-sparing sugery). The clinical and radiological features may be helpful in characterization of the cystic lesions of the kidney, but only pathological examination can establish the definite diagnosis.

E-PS-18-002
Anastomosing hemangioma of the kidney: Diagnostic pitfalls and review of the literature

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Objective: Vascular lesions of the genito-urinary(GU) tract are overall infrequent. Anastomosing hemangioma(AH) is a poorly recognized neoplasm with strong proclivity for GU organs and may simulate angiosarcomas. We aim to present a case of AH of the kidney, followed by a review of all cases reported in literature.
Method: A 63-year-old male was referred to our Institution with a 4 months history of hematuria and dysuria. Computed tomography(CT) showed a mass in the right kidney pelvis suggestive of urothelial neoplasm.
Results: Nephrectomy specimen showed a 5x3.5 cm well-demarcated nodule in the upper renal pelvis, with a spongy, mahogany-reddish appearance. The lesion was composed of anastomosing sinusoidal capillary-sized vessels arranged in a lobular architecture, with scattered hobnail endothelial cells exhibiting minimal cytological atypia, along with non-endothelial supporting-cells. Focal aspects included areas of moderate/high cytological atypia, vascular thrombi and extramedullary hematopoiesis. Immunohistochemistry revealed positivity for vascular markers and a proliferative index(Ki67) <1 %. Medline search revealed 117 cases of AH overall, 61(52.1 %) occurring in GU organs (56 in kidneys, 1 in bladder, 4 in testis/paratestis).
Conclusion: AH is a rare entity and it may raise the concern for angiosarcoma. Pathologists should be aware of this hemangioma variant in order to avoid overdiagnosis of angiossarcoma.

E-PS-18-003
Postpubertal teratoma with somatic-type malignancy in the form of Primitive Neuroectodermal Tumour (PNET): A case study with focus on diagnostic pitfalls and the relevance of reporting this tumour subtype

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Objective: Somatic-type malignancy(SM) within testicular germ cell tumours(TGCTs) is a rare event. It occurs more commonly in metastatic sites after chemotherapy (conveying poor prognosis), but may also present in the testis, mainly in the context of postpubertal teratomas(TE). We aim to present a case of a TE with SM in the form of PNET, focusing on diagnostic pitfalls and literature review.
Method: A 52-year-old male presented with diffuse enlargement of the left testis. Positron emission tomography(PET) favored a malignant testicular neoplasm with mesenteric lymphadenopathies.
Results: Morphology and immunohistochemistry on testicular biopsy suggested a small-cell neuroendocrine carcinoma. The orchiectomy specimen, weighing 576 g and measuring 13x11x8.5 cm,

was completely occupied by a solid, white, rubbery mass, with areas of necrosis and hemorrhage, which invaded the epididymis and the mediastinum testis. It had a solid and infiltrative growth pattern, exhibiting small blue round cells, crushing artefacts, rosette formation and severe cytological atypia. Positivity for CK8/18 and Synaptophysin(focal), CD99 and CD56(strong and diffuse) was depicted.
Conclusion: Surgical resection is the treatment of choice for most cases of SM given their chemo-resistance. However, Pathologists should be aware of PNET SM and report it, as PNET-specific chemotherapy was shown to be effective in treating this TGCT subtype.

E-PS-18-004
Clinical case of multifocal primary tumour: Is the additional examination of the body required in case of malignant tumour of the urinary bladder?
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Objective: To determine the histogenesis of the urinary bladder (UB) neoplasia under suspected risk of multifocal pathology.
Method: Histological and immunohistochemical (IHC) examinations were carried out in several stages: 1) Hematoxylin and eosin; 2) CKpan, CD45 and Vimentin; 3) CKLMW, CKHMW, CK7 and 20; 4) AR, PSA, AMACR.
Results: The first stage, presented by histological examination of the formation in the UB revealed the growth of the undifferentiated malignant tumour. At the same time, the lesions with tubular-trabecular nature were revealed. For better understanding of the tumour nature the IHC examination (2,3,4 stages) was carried out. The second stage of IHC showed the epithelial nature of both malignant tumours (CKpan« + », CD45«-», Vimentin«-»). The third stage showed that the tissue of adenocarcinoma of the prostate was heterogeneously positive for CKLMW«+/-» and negative for CKHMW, CK7 and 20, but the tissue of undifferentiated UB tumour expressed all types of CK. The fourth stage of IHC showed that in the tissue of adenocarcinoma the reaction was positive for AR, PSA, AMACR and in undifferentiated UB tumour it was negative for AR and PSA and heterogeneously positive for AMACR«+/-». By comprehensive study the final diagnosis was determined: combined malignant tumour—invasive urothelial carcinoma of the UB and prostate acinar adenocarcinoma (9(5 + 4) according to D.F.Gleason).
Conclusion: This clinical case demonstrates the development of multifocal malignant pathology with lesions of the urinary bladder and prostate. With the presence of the urinary bladder carcinoma, another malignancy can develop within the same topographic area or other systems. For better differentiation of tumour histogenesis the comprehensive histological and immunohistochemical examinations are required.

E-PS-18-005
Histological features with prognostic significance in testicular germ cell tumours
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Objective: Our study aims to identify histological features with prognostic and/or predictive role which may be further used to build a score system to inform clinical decision.
Method: We assessed 39 cases of testicular germ cell tumours (TGCTs), focusing on the following particular features: quantification of different tumour subtypes, presence of intratubular germ cell neoplasia, histological pattern, cytoplasm appearance, nuclear pleomorphism, mitotic index, tumour necrosis, inflammatory lymphocytic infiltrate. These variables were analyzed in relationship with several clinicopathological characteristics and patients' outcomes. For statistical analysis we used exact tests and Spearman's rho.
Results: The presence of multiple tumour subtypes increased the risk for distant metastases. The glandular pattern was correlated with a better overall survival (OS) as compared to the papillary pattern that increased the risk of death. Cellular pleomorphism was negatively correlated with OS. No similar results were obtained for a high mitotic index. The presence of acidophilic cytoplasm could predict the global therapeutic response rates. The lymphocytic infiltrate, assessed through its qualitative and quantitative expression, could be proposed as a prognostic and predictive marker.
Conclusion: The evaluation of several non-conventional histological features in TGCTs offers complementary data to optimize the prognostic stratification and guide the therapeutic decision.

E-PS-18-006
A case report of a primary renal well differentiated neuroendocrine tumour
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Objective: A 58 year old man suffering from recurrent swelling of his legs and losing weight in the last few months. Direct physical examination was unremarkable, his laboratory values showed decreased hemoglobin (9.57 G/dl), increased WBC (10.2x1000, 80 % neutrophils), proteinuria, and normal Urea and Creatinine. CT scan revealed a mass involving the inferior lobe of the right kidney measuring 7 cm in greatest dimension. Right nephrectomy was performed on the patient.
Method: Gross examination showed a white-beige solid and well demarcated tumour, the renal tissue looked normal. The applied sections showed proliferation of packed trabeculae, nests and cords of cells having eosinophilic granular cytoplasm and uniform nuclei with stippled chromatin, no mitotic activity neither necrosis could be seen despite generous sampling. The tumour growth was limited to the renal borders.
Results: Immunohistochemistry revealed positive staining for CD99, Chromogranin, and negative result for CD10 and CK7 with positive internal control, Ki-67 showed very low index (<1 %).
Conclusion: Microscopic morphology and the applied immunohistochemistry were consistent with well differentiated neuroendocrine tumour (carcinoid).

E-PS-18-007
Retroperitoneal and pulmonary metastases from burned-out testicular germ cell tumour as initial clinical presentation: Report of two cases
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Objective: To present two cases of metastatic deposits from burned-out testicular germ cell tumours (GCTs) as initial clinical presentation of the disease.
Method: Case 1: Retroperitoneal necrotic tumour from a 40-year old male patient, and fragments from the lumbar vertebra were submitted for analysis. Case 2: Core biopsy of a lung mass from a 26-year old male patient was received for analysis. Both cases were routinely processed and additional immunoihistochemical analyses were performed.
Results: Case 1: Necrotic retroperitoneal tumour had only a few vital germ cell tumour cells positive for PLAP and CD30. In the testis, an area measuring 17 mm showed hyalinization, sclerosis and calcification with cystic structures presenting mature teratoma positive for cytokeratins 7

and 20. In the surrounding area, a component of germ cell neoplasia in situ (GCNIS) positive for PLAP was found. Case 2: Lung core biopsy reveled 1 mm focus of of embryonal carcinoma, positive for PLAP, CK7 and CD30. Testicular tissue had areas of GCNIS positive for PLAP and c-kit and 8 mm focus of hyalinization and calcification.
Conclusion: Testicular burned-out (GCT) is a rare neoplasm that initially manifests as metastatic deposits in the retroperitoneum and lung. Awareness of this phenomenon is mandatory in diagnosis of metastatic deposits.

E-PS-18-008
Large osteoblastic metastasis to the sphenoid bone in a 62-year-old man - a rare first manifestation of prostate cancer
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Objective: Introduction: Prostate cancer is the second most common cancer in men. We present a case of a 62-year-old man with massive metastasis of prostate cancer to the sphenoid bone causing left-sided visual loss and exophthalmos as the first symptoms of the disease.
Method: N/A
Results: Case report: The patient consulted a neurosurgeon due to the left eye blindness with ocular proptosis without any other neurological symptoms. CT examination of the head revealed a tumour of the middle cranial fossa infiltrating the orbit. Histopathological examination of the collected specimens revealed massive invasion of poorly differentiated carcinoma, which immunohistochemical profile matched prostatic adenocarcinoma (PSA(+), AMACR(+), prostein (+)). Analysis of the immunophenotype of cancer cells excluded the primary tumour of glial or meningothelial origin. Further diagnostic tests revealed increased serum PSA (46.7 ng/ml), numerous enlarged paraaortic lymph nodes, hypodense lesion in the liver and massive metastatic lesions in bones of the pelvis. Hormonal therapy resulted in an initial 4-fold decrease of serum PSA, followed by another rise after 4 months. The patient is currently treated at the Chemotherapy Clinic at the University Hospital, Wroclaw.
Conclusion: Conclusions: Prostate cancer metastases should be always considered in males with focal neurological symptoms and in histopathological diagnosis of intracranial tumours.

E-PS-18-009
Fetal rhabdomyomatous nephroblastoma in an adult: A rare entity with a challenging diagnostic
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Objective: Fetal rhabdomyomatous nephroblastoma (FRN) is a rare variant of Wilms' tumour with only few cases reported in the literature. Its occurrence in an adult is exceptional.We report a new case in order to illustrate clinical and histopathological features of this entity.
Method: In this study, we present a case of FRN diagnosed in our pathology department.
Results: A 31-year-old-woman was hospitalized with haematuria and left lumbar swelling. Physical examination revealed a left lumbar mass. Ultrasound and computed tomography evidenced a well-circumscribed-15 cm-heterogenous-tumour involving the upper-renal-pole. Magnetic resonance imaging showed asolid-left-renal-tumour measuring 15× 10,5× 9 cm and containing numerous cystic changes. The diagnosis of nephroblastoma was suggested. A left nephrectomy was immediately performed. The tumour was witishon cut-surface with whorled aspect and several cystic and myxoïd changes. Histopathologically, the tumour was well-circumscribed mostly composed of mesenchymatous component with fetal-striated-muscle-cells in a myxoïd background. Both blastemal and epithelial components could not be demonstrated. The diagnosis of FRN was made. After a 3 month follow-up, no metastases or recurrences were detected.
Conclusion: FRN is a rare variant of nephroblastoma with distinctive clinical, pathological and behavioral features. Unilateral FRN have generally favorable outcomes when surgically treated since they are poorly responsive to chemotherapy.

E-PS-18-010
Primary small cell carcinoma of the urinary bladder: A case report
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Objective: Extrapulmonary Small Cell neuroendocrine carcinoma of bladder is a very rare and highly aggressive tumour which usually diagnoses at advanced stages. The origin and pathogenesis of the disease is unknown. We present a case of primary small cell carcinoma of the urinary bladder with explanation of histopathologic and immunohistochemical characteristics.
Method: The Patient is a 75-year-old-man with gross hematuria. Abdominopelvic CT-scan showed an irregular non-enhanced filling defect on posterior wall of urinary bladder. On cystoscopic examination a large vegetative mass measuring 8 cm in maximal diameter was identified on posterior wall. Cystoscopic biopsy performed. Primary pathology report was poorly differentiated carcinoma with invasion into muscularis propria. Radical cystoprostatectomy was done for the patient.
Results: Histopathological examination of the radical cystoprostatectomy showed sheets of small tumoural cells extensively infiltrating the bladder wall, prostate, seminal vesicle and lymph nodes. Immunohistochemical staining showed positivity of tumoural cells with CD56, dot-like positivity for pan-Cytokeratin and focally positive synaptophysin. Ki67 labeling index was positive in about 80 % of tumour cells. Tumoural Cells were negative for chromogranin and LCA which confirmed widespread poorly differentiated small cell neuroendocrine carcinoma.
Conclusion: Presented case is a rare case of aggressive primary Small Cell Carcinoma of urinary bladder with extensive metastasis.

E-PS-18-011
Incidental high grade urothelial carcinoma in a hydronephrotic, nephrolithitic, non functioning kidney: A case report from a medical institute of Rohilkhand region, India
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Objective: To report an incidental finding of high grade urothelial carcinoma in a hydronephrotic, nephrolithitic, non functioning kidney.
Method: Formalin fixed right nephrectomy specimen was processed as per protocol. Hematoxylin and Eosin stained sections were observed microscopically. Relevant immunohistochemical stains were ordered for representative sections. Clinical details and investigations were retrieved from patient's case file.
Results: A 55 year old male presented with right flank pain. There was no gross or microscopic hematuria. Ultrasonography revealed hydronephrosis with nephrolithiasis. Renal diethylenetriaminepentaacetic acid (DTPA) scan showed severely impaired renal function. Clinically diagnosed with right non functioning kidney with calculi and hydronephrosis, the patient underwent right nephrectomy. Macroscopic examination revealed distorted calyces, impacted stones and a tan-white solid area measuring 8 cm × 7 cm. Microscopically, the patient was diagnosed with high grade urothelial carcinoma infiltrating into the renal capsule and perinephric fat. Immunohistochemistry was positive for Anti-

p63, high molecular weight cytokeratin, pan cytokeratin, CK 7, CK 5/6 and patchy positive for CK 20.
Conclusion: Non functioning kidney with nephrolithiasis and hydronephrosis can masquerade renal urothelial carcinomas. Hematuria, although the most common symptom of renal malignancies may not be present in all cases. The present case necessitates clinicians and pathologists to review their approach towards diagnosis and management of such cases.

E-PS-18-012
Nested variant of urothelial cell carcinoma of urinary bladder: A case report
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Objective: The aim of this report was to present the clinicopathological and immunohistochemical features of a rare variant of the urothelial cell carcinoma, nested variant.
Method: A 71 years old male presented with a 2 months history of hematuria, dysuria and lower abdominal pain. The patient underwent transurethral resection. He died 2 months after diagnosis.
Results: Histologically, tumour was composed of nests of tumour cells, showing moderate nuclear and cellular atypia, which increases in the deeper aspects of tumour, especially in the nests of tumour cells extended through the detrusor muscle present in the specimen (pT2). Notable inflammation was present in stroma. Immunohistochemistry showed positivity for p63, p53, p21 and pan-keratins (CK7, CK20, Ck-MNF, CK 19, CK34bE12) as well as EMA. Proliferation index assessed by Ki-67 was 30 %. Tumour cells were negative for S100, neuroendocrine markers (chromogranin, synaptophysin, NSE), PSA, CD44, CD10, CEA and CA19-9.
Conclusion: Ki-67 and p53 positivity are indicators of the disease progression. Despite bland appearance, the nested variant of urothelial carcinoma has an aggressive biological behavior. The majority of patients presents at the advanced stage and have a poor outcome.

E-PS-18-013
Lemphoepithelioma like urothelial carcinoma of the urinary bladder
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Objective: Lemphoepitethelioma like carcinoma has recently been described as a distinct variant of urothelial carcinomain the urinary bladder. This rare type of carcinoma may be pure, predominant or focally admixed with the other types of urothelial carcinoma.When it is pure or predominant the lemphoepithelioma like carcinoma of theurinary bladder has a relatively favorable prognosis. We report two cases of lemphoepithelioma like carcinoma in theurinary bladder.
Method: Case 1: A 34-year old female was admitted with a history oflemphoepithelioma like carcinoma in theurinary bladder stage III. Case 2: A 68-year old male was admitted because of haematuriaand lemphoepithelioma like carcinoma in theurinary bladder stage III.The patient had a past history of urothelial carcinoma of the urinary bladder 6 months ago.
Results: Partial cystectomy was performed and the histological examination showed pure lemphoepithelioma like carcinoma in the female patient and predominant lemphoepithelioma like carcinoma in the male patient.
Conclusion: Early detection of these neoplasms could identifitytumours which might be sensitive to chemotherapeutic agents.

E-PS-18-014
Testicular pure cartilaginous teratoma: A case report
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Objective: The monodermal teratomas are rare tumours of the testis which frequency ranges from 2,7 to 7 %. The testicular pure cartilaginous differentiated teratoma is exceedingly rare, with only few cases previously descbribed.
Method: A 45-year-old man visited our hospital complaining of painful swelling of the scrotum contents. Clinical examination and Imaging analysis revealed a mass in his right testis without evidence of metastatic disease. Blood chemistry showed normal levels of AFP and B-HCG. Therefore high inguinal orchiectomy was performed.
Results: The cut surface of the testis showed a 8 × 7 × 5 cm circumscribed, white-gray, solid, lobulated tumour located within the testicular parenchyma. Microscopically the tumour was entirely composed by mature cartilage. No intratubular germ cell neoplasia unclassified type was visible. The patient is alive with no evidence of disease at follow up of 21 months.
Conclusion: The preoperative recognition of these tumours might help urologists approach the patients conservatively.

E-PS-18-015
Bladder sarcomatoid carcinoma in a 36 year old woman: A case report
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Objective: In pregnancy, malignant tumours are uncommon with an incidence between 0.02 and 0.1 %. Sarcomatoid carcinoma is a rare tumour of unknown histogenesis, with an incidence of 0.31 % of all bladder tumours. The prognosis is poor; approximately 66 % of these tumours develop metastases within 1 year. This tumour appears more frequently in men with a mean age of 70 years, we present a case in a woman of 36 years in the puerperium.
Method: The patient had symptoms of urinary tract infection with worsening of the condition, an exploratory laparotomy were performed.
Results: A biopsy was performed; we observed an atypical squamous cell proliferation with a malignant stromal component, with presence of mitosis and foci of necrosis. The tumour showed expression of Ck5/6, CkAE1-AE3, p63 and vimentin. After the excision of the piece, infiltration of the muscle itself and perivesical fibroadipous tissue were observed. Palliative chemotherapy was initiated.
Conclusion: The diagnosis of sarcomatoid carcinoma in a biopsy material is difficult, due to the morphological variability of this neoplasia, which not always allows its exact diagnosis. It is assumed that a genetic mutation occurs at an early stage of its carcinogenesis, however further studies are needed to clarify the origin of this.

E-PS-18-016
Squamous cell carcinoma (SCC) of the renal pelvis: A rare neoplasm
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Objective: Primary squamous cell carcinoma (SCC) of the renal pelvis is rare accounting for only 0.5 % to 0.8 % of malignant renal tumours. Nephrolithiasis, especially formation of staghorn calculi, is the most

common risk factor for SCC, which usually occurs in older adults (age 50–70 years) with no sex predilection.
Method: A 63-year-old male presented with complaints of pain in bilateral flank region over 3 months with an associated history of significant weight loss. During the radiologic investigation, a renal mass was detected in the right kidney and the patient underwent a right radical nephrectomy. On gross examination the specimen was found to be enlarged measuring 13 × 10 × 8 cm. On gross section the entire renal parenchyma and renal pelvis were replaced by a 6 × 6 × 5 cm whitish grey mass.
Results: Microscopic examination revealed a poorly-differentiated SCC infiltrating the kidney parenchyma and perinephric-pelvic fat. The tumour invaded the renal capsule, perirenal fat and lymphovascular structures and presented large areas of necrosis
Conclusion: Most renal SCCs are moderately or poorly differentiated and typically present at an advanced stage-pT3 or higher. Surgery is the mainstay of treatment while adjuvant treatments have marginal benefit. The prognosis is dismal with a 5-year survival rate of less than 10 %.

E-PS-18-017
Proximal-type epithelioid sarcoma of the scrotum, a case report
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Objective: Proximal-type epithelioid sarcoma is a rare soft tissue tumour, which should differentiate from other epithelioid neoplasms such as extrarenal rhabdoid tumour, malignant melanoma, and undifferentiated carcinoma .
Method: A 28-year-old man presented with rapid growing scrotal mass for a few months. Physical examination revealed adult fist sized masses in the right scrotum and inguinal area. An abdominopelvic computed tomography showed ill-defined heterogeneously enhancing mass in the right scrotum and well-defined enhancing mass in the right inguinal area, which thought to be a metastatic lesion. He underwent radical orchiectomy and inguinal lymph node dissection.
Results: Microscopically, the mass was exclusively composed of large epithelioid cells, which show prominent nucleoli and abundant eosinophilic cytoplasm. Immunohistochemically, epithelioid cells were immunopositive for cytokeratin, vimentin and CD34 but not for INI-1, which was consistent with epithelioid sarcoma.
Conclusion: Since there are some sharing histomorphologic features between epithelioid neoplasms, immunohistochemical stains for cytokeratin, EMA, vimentin, CD34, INI-1, myogenic markers, S-100, melan-A, and angiogenic markers are needed to make a diagnosis. We report a rare case of proximal-type epithelioid sarcoma in the scrotum with metastatic lesion in the inguinal lymph node.

E-PS-18-018
Solitary fibrous tumours of the prostate: A case report
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Objective: Solitary fibrous tumour (SFT) is a rare spindle cell neoplasm most frequently found in the pleura, however it can be seen in other sides such as urogenital tract. Prostate is a rare location of this tumour. Differential diagnosis should consist of stromal tumour of uncertain malignant potential of the prostate (STUMP), stromal sarcoma, leiomyosarcoma and gastrointestinal stromal tumour because of different histological patterns and localisation.
Method: We report a case of prostatic SFT in a 79-year-old man who presented with obstructive urinary symptoms. The case was initially diagnosed as benign prostatic hyperplasia. A transurethral resection of prostate was performed.
Results: Histopathological analyses showed that the tumour composed of fibroblast like cells with patternless pattern, thick bands of collagen and prominent branching, hyalinized vessels. Immunohistochemistry demonstrated expression of CD34, CD99, bcl-2, vimentin, progesterone but no expression of desmin, smooth muscle actin, CD31, S100, c-kit. The patient was not operated due to cardiovascular problems but he is still alive, 5 months after diagnosis.
Conclusion: Although the clinical outcome of prostatic SFT seems favourable, it remains difficult to predict, therefore postoperative long-term follow-up is important. Furthermore, the diffferantial diagnoses of SFT from other spindle cell lesions on prostate is necessary.

E-PS-18-019
Paratesticular malignant mesothelioma: A challenging diagnostic of unusual tumour. Report of two cases
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Objective: Paratesticular malignant mesothelioma (PMM) is a rare tumour, originating in the mesothelial cells of the tunica vaginalis. We present two cases of PMM without history of asbestos exposure, in order to reveal its anatomopathological characteristics and diagnostic keys.
Method: CASE 1. A 83-year-old man followed in consultations by right hydrocele. During surgery, testis and epididymal stones are observed, radical orchiectomy is decided. CASE 2: A 71-year-old man, who has thickening and irregularity of the left testicle. Ultrasound reveals cysts of the epididymis with intracystic papillary lesions, is removed.
Results: In the histological sections, epithelial proliferation is observed, with papillary growth pattern, which infiltrates the tunica albuginea, with vascular permeation, in the first case. The immunohistochemical study demonstrates its mesothelial derivation, with positivity for calretinin, WT1 and podoplanin (D2-40). CASE 1. Two years later, recurrence in the inguinal canal with right retroperitoneal adenopathies; and erythematous and indurated plaques on prepubic and scrotal skin. Diagnosis of recurrent mesothelioma in the right groin with cutaneous metastases. He died 2 years later. CASE 2. Without relapse in the present.
Conclusion: PMM is a very rare tumour, therefore its difficult to diagnose. Given its poor prognosis, its accurate diagnosis is of utmost importance.

E-PS-18-021
Malignant sertoli cell tumour of the testis mimicking seminoma
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Objective: Malignant sex cord Sertoli cell tumour of the testis is a rare neoplasm which represents less than 1 % of all testicular neoplasms.
Method: An orchiectomy specimen was received in formalin and a testicular tumour was detected. H + E, PAS, PAS-D and immunohistochemical stains were conducted in order to identify the tumour.
Results: Macroscopically the tumour was firm, white coloured, measuring 6X4,5X4 cm. Microscopically the tumour consisted of large cells with clear cytoplasm, diffusely infiltrating the testis. Lymphocytic infiltration of the tumour, fibrosis of the stroma and lymphovascular invasion was also observed. The neoplasm infiltrated the tunica albuginea, tunica vaginalis, the rete testis and the spermatic cord. Initially the possibility of a tumour representing seminoma was suggested. The tumour cells were negative for Oct3/4, podoplanin, PLAP, CD117, AFP, hCG, CKAE1/

AE3, synaptophysin, chromograninA, MelanA, HMB45, EMA while stained positive for InhibinA, vimentin and calretinin. The cytoplasm was focally PAS positive, without diastase resistance. A diagnosis of a malignant sex-cord stromal tumour was made most likely representing a Sertoli tumour.
Conclusion: Sex-cord Sertoli cell stromal tumours should always be considered in the differential diagnosis of clear cell malignant tumours of the testis.

E-PS-18-022
Schistosomiasis-induced squamous cell bladder carcinoma: A case report
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Objective: Urogenital schistosomiasis (UGS) is a chronic infection caused by the human blood fluke Schistosoma haematobium. Schistosoma haematobium is a known risk factor for cancer leading to squamous cell carcinoma (SCC) of the urinary bladder. However, the cellular and molecular mechanisms underlying UGS-induced carcinogenesis have not been well defined.
Method: A 75-year-old Syrian patient presented with macroscopic hematuria and pelvic pain to urology clinic. At ultrasound imaging irregularity in the bladder mucosa was detected and transurethral resection (TUR) was performed.
Results: On routine histological examination of TUR specimen a tumour that arises in epithelium, infiltrates in sheets, nests and islands, including formation of keratin pearls was seen. Tumour cells were polygonal with well defined cell borders, amphophilic to eosinophilic cytoplasm, pleomorphic, occasionally bizarre, nucleus with irregular chromatin and prominent nucleoli. An ınflame tissue that contains Schistosoma eggs were noted. The diagnosis was SCC and Schistosoma cystitis.
Conclusion: Schistosomiasis is the second most common socioeconomically devastating parasitic disease after malaria, affecting about 240 million residents of developing countries. Most affected individuals are asymptomatic. Eggs deposited in the bladder wall resist elimination by type 1 T lymphocytes. Progressive bladder disease results in obstructive uropathy and predisposes to (mostly) SCC.

E-PS-18-023
Renal cell carcinoma or fat-poor angiomyolipoma?
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Objective: Angiomyolipoma belongs to a family of neoplasms called perivascular epithelioid cell tumours (PEComas), composed of an admixture of blood vessels, smooth muscle and mature adipose tissue. 3–4 % of angiomyolipomas exhibit no detectable fat at CT and are almost radiologically indistinguishable from other renal tumours, including renal cell carcinoma (RCC). We report a case of a 66-year-old woman with a mass at the lower pole of the left kidney. The tumour considered by radiologists as a renal carcinoma and surgical excision was performed.
Method: We received a well-circumscribed kidney tumour measuring 3,2 × 3 × 2,8 cm.
Results: Microscopically the tumour consisted of spindle cells with microvesicular clear to pale eosinophilic cytoplasm, round to oval nucleus, mild to moderate pleomorphism and rarely lipomatous differentiation. Immunohistochemically, they stained positive for Vimentin, SMA, HHF-35, Calponin, HMB45, Mart1, focally for ER, PgR and negative for RCC, CD10, S100 and CKAE1/AE3. The mitotic rate was 1 mitosis / 50 HPF. The presence of fat was highly suggestive of angiomyolipoma.
Conclusion: Renal angiomyolipoma is an uncommon benign tumour, its proportions of smooth muscle and fat appear to be associated with their location in the renal parenchyma and may present a challenge for clinical and pathological diagnosis.

E-PS-18-024
Urachal remnants in a urinary bladder with non-invasive papillary carcinoma and in situ urothelial carcinoma
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Objective: To present a case of urachal remnants located in the muscularis propria of a cystoprostatectomy specimen, which are clinically important when complicated by infection, neoplasia or cystic dilation.
Method: A 60yo male patient was diagnosed with infiltrative urothelial carcinoma invading the lamina propria and high-grade papillary carcinoma, after examination of transurethral biopsy specimen. Three months later the patient underwent cystoprostatectomy. Macroscopic examination revealed a tumour of the bladder dome and a whitish-reddish lesion of the right lateral wall measuring 2,5X2,3X0,8 cm and 2,3X1,2 cm respectively.
Results: Microscopically the tumour was a high-grade papillary urothelial carcinoma, while the lesion corresponded to in situ urothelial carcinoma. Underlying the papillary carcinoma, cyst like spaces were observed in the muscularis propria. These were lined by cytologically benign urothelial cells. The cells were positive for CK7 and negative for CK20 and p53. The basal cells were positive for p63 and the proliferative index (Ki67) was low. These findings were compatible with benign urachal remnants.
Conclusion: Urachal remnants are ordinarily small, multilocular, asymptomatic and consist of tubular structures and canals usually lined by urothelial, cuboidal, flat or atrophic cells, surrounded by a thin fibromuscular layer. Awareness and correct identification of urachal remnants is important, in order to avoid diagnostic pitfalls.

E-PS-18-025
Primary micropapillary carcinoma of the urinary bladder: A rare entity
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Objective: Micropapillary carcinoma is an uncommon variant of urothelial carcinoma which has been associated with a higher stage at diagnosis and increased risk of metastatic disease, even if it comprises only a small fraction of the overall tumour volume.
Method: We report the case of a 81-year-old man who presented with macroscopic heamaturia. MRI imaging revealed a tumour in the posterior wall of the bladder. Transurethral biopsy showed a high-grade micropapillary carcinoma with muscle invasion.
Results: Microscopically, the malignant cells were arranged in small papillary clusters or tightly cohesive nests lying in clear spaces, exhibited high-grade nuclear features. Conventional transitional cell carcinoma elements were not found. The immunohistochemical profile (positivity for p63, cytokeratin 7 and cytokeratin 20) suggests an urothelial origin. Due to other health problems, the patient received only actinotherapy, with no tumour recurrence or metastasis after 4-months follow-up.
Conclusion: In conclusion, we present a rare case of primary micropapillary carcinoma of the urinary bladder. In such cases, pulmonar and peritoneal origins must be excluded. Although its rarity, it should be kept in mind when dealing with high-grade urothelial tumours, because

even focal presence of micropapillary pattern in an otherwise conventional urothelial carcinoma, is associated with advanced tumour stage and poor prognosis.

E-PS-18-026

A benign tumour of the epididymis; Leiomyoma; Case report

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Objective: Epididymal tumours are very rare with the rate of 5 % of intrascrotal tumours and 75 % of them are benign. The most frequent benign tumours are adenomatoid tumours and leiomyomas.
Method: Case Report: Our patient is a 41-year-old man. He was admitted to urology clinic with a 1-year history of a slow-growing, painless mass in his left scrotum. Ultrasonographic examination revealed a well-circumscribed, solid, hypoechoic mass with a diameter of 1,5 cm in his left epididymis. The mass at the tail of the epididymis was excised with its well-circumscribed borders.
Results: The histopathological evaluation; revealed a well-circumscribed neoplastic proliferation of spindle cells with deeply eosinophilic, fibrillar cytoplasm arranged in intersecting fascicles. Nuclear atypia, mitosis or necrosis were not present. The neoplastic cells showed strong cytoplasmic staining for desmin, Smooth-muscle-actin(SMA) and Caldesmon. As Ki-67 proliferation index was 1 %, the lesion was diagnosed as Epididymal Leiomyoma(EL).
Conclusion: EL is a benign tumour that can be cured through simple, organ-preserving surgical excision. It is the second most common neoplasm of the epididymis, following adenomatoid tumour and represents 6 % of primary epididymal tumours. Although it is a rare lesion, EL should be considered in differential-diagnosis of scrotal masses in order to provide testicular preservation.

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Concordant occurrence of RCC and angiomyolipoma in the same kidney

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Objective: Angiomyolipoma is a rare tumour often associated with tuberous sclerosis. Although its clinical course is usually benign, it may be associated with various adverse outcomes.
Method: A 52-year-old female patient underwent nephrectomy due to kidney tumour. Two histologically different tumours were found directly next to each other. RCC was 3.5 cm in diameter (pT1aNXMX, G3) and angiomyolipoma diameter was 7 cm.
Results: Both tumours were c-Kit and CK20 negative, and Vimentin positive. Angiomyolipoma showed immunohistochemical positivity to the MSA, SMA, HMB45, Melan A and CK AE1 / AE3, while it was negative for EMA, RCC and CK7. Renal cell carcinoma showed immunohistochemical positivity for EMA, RCC, CK AE1 / AE3 and CD10 and focal positivity for CK7, while being negative for MSA, SMA, S-100, HMB45 and Melan A.
Conclusion: The paper presented a rare example of simultaneous appearance of two histologically and immunohistochemically different tumours in the same kidney, which were observed and documented with extensive immunohistochemistry.

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Nephrogenic adenoma of the prostatic urethra: A case report

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Objective: Nephrogenic adenoma(NA) is a rare proliferative lesion of the urothelium. It is described in the urinary bladder. Nonspesific symptoms such as hematuria, dysuria and bladder-irritability are the most frequent complaints of the patients.
Method: Case Report: Our patient is a 64-year-old man. He was admitted to urology clinic with the complaints of dysuria, pollakuria and frequency continuous for 2 weeks. He had a history of transurethral-resection(TUR) for prostatic nodular hyperplasia. Cystoscopy was performed and small suspicious papillary-lesions in the prostatic urethra were noticed and TUR was applied.
Results: In the histopathological evaluation; tubular structures lined by cubic-epithelium and vascular-like tubules lined by flattened epithelial cells or mucin containing signet-ring like cells in between the prostatic glands were seen. There was no cellular atipia and mitosis. As P63, High-Molecular-Weight-Cytokeratin(34bE12) and AMACR(alpha-methylacyl-CoA-racemase) were positive in the lesion, it was diagnosed as NA.
Conclusion: NA; which can be seen anywhere with urothelial-lining, is accepted as a reactive-lesion caused by a previous damage (trauma,TUR, surgery for lithiasis, renal-transplantation, etc.). As it is a benign condition, no treatment is needed after the excision for the diagnosis. It is rarely seen in prostatic-urethra; however should be considered in differential-diagnosis of suspicious-papillary lesions of the urothelium.