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Pathophysiology, Diagnosis, and Initial Management

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Abstract

The rate of cancer patients will continue to increase in the coming decades. Additionally, new treatments will continue to emerge. The increased survival rates and the anti-tumour medications used will without doubt contribute to an increased rate of patients with oncological emergencies. Patients with oncologic emergencies will foremost seek care at an emergency department, but physicians at other clinics should also be familiar with the initial management of these patients. The initial management of any critically ill and instable patient, including those presenting with an oncologic emergency, should be based on the O-ABCDE approach and aimed at countering established or potentially life-threatening conditions. Oncologic emergencies can be divided into several different categories. This chapter focuses on five different oncologic emergency categories: metabolic, haematological, cardiovascular, neurologic, as well as treatment related. While all critically ill patients with an oncologic emergency must be attended to based on the O-ABCDE approach; it is of vital importance for the treating physician to also treat the patients symptomatically and at the same time rule in or rule out other differential diagnosis.

Keywords

Emergency medicine · Initial management · Malignancy · Oncologic emergency · Oncology

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1 Introduction

Cancer continues to be a significant public health issue globally and is a major cause of death (Siegel et al. 2019). The World Health Organization (2020) reports that in 2018, over 18 million individuals worldwide were diagnosed with cancer and that close to 10 million lost their lives to the disease. Furthermore, it is believed that the rate of individuals with cancer will continue to increase. The estimated number of new cancer cases in 2040 is just above 30 million (International Agency for Research on Cancer 2022).

During the last two decades, the mortality rate in cancer, internationally, has though been declining (Hashim et al. 2016). The decrease is seemingly partly related to improvements in the health care contributing to a faster and earlier diagnosis of cancer and partly due to a prompter aggressive intervention with both conventional anti-cancer treatment like chemotherapy as well as new medications like immunotherapy. The increasing rate of new cancer cases, more modern anti-cancer treatments, and not least an improved survival rate will most likely contribute to a higher number of oncologic emergencies.

Oncologic emergencies are potentially life-threatening conditions which may present at any time during the course of a patient's cancer disease. It may very well be the initial manifestation of their cancer (Grasso et al. 2007), occur because of the underlying tumour/cancer disease (Shinagare et al. 2011), or be a consequence of the received cancer treatment (Lyman et al. 2014). It is therefore imperative that physicians are familiar with oncologic emergencies. Another reason for having this knowledge is that many cancer treatments have been centralised (Kilsdonk et al. 2018). This may therefore cause the cancer patient to seek health care for their cancer-related issues as well as oncologic emergencies, in other cities, clinics, and hospitals than the one where they are primarily treated for their cancer.

A systematic review from 2017 showed that cancer patients are common in emergency departments (ED) and that the incidence of their ED visits exceed those of the general population (Lash et al. 2017). Depending on the cohort examined and the objectives studied, different figures and rates of cancer patients in the ED are presented. Several studies though have shown that it is common for cancer patients to seek emergency care at the ED during their illness (Barbera et al. 2010; Mayer et al. 2011; Leak et al. 2012). In a large study on US EDs by Rivera et al. (2017), it was shown that between 2006 and 2012, 4.2% of all adult ED visits (n= 696 million) were conducted by an individual with a cancer diagnosis. The same study showed that the admission rate from the ED for cancer patients was far larger (59.7%) than those with no cancer-related visits (16.3%). Other studies have shown that between 12% and 15.4% of all cancer patients being admitted to the intensive care unit are admitted via the ED (Taccone et al. 2009; Soares et al. 2010).

Knowledge of oncologic emergencies is thus of vital importance for all physicians, not least those in the emergency department which most likely will encounter these patients seeking for different emergency symptoms. This chapter will provide an overview of oncologic emergencies at the ED and its management. However, it can also be used by other physicians as well in order to manage patients with oncologic emergencies at their clinics.

2 Initial Management of the Acutely Ill Patient

The initial management – assessment and treatment – of any emergency patient must be based on the ABCDE approach. This approach can be used for all ill patients inclusive those being the victim of a physical trauma. The trauma-interested reader is referred to the Advanced Trauma Life Support (ATLS) per the American College of Surgeons (2022). In this chapter, the focus will be the acutely ill nontrauma patient.

The ABCDE approach is aimed to systematically evaluate and parallelly treat an acutely ill patient. This approach effectively identifies different lethal and potentially lethal conditions during the evaluation thus contributing to a prompter treatment. Another important aspect of using the ABCDE approach is to minimise the risk of premature closure[1] and thus the risk of missing other important and possibly life-threatening conditions.

To make the ABCDE approach more efficient and safer for the patient, an O has been placed in front of the ABCDE making it the O-ABCDE approach. The acronym stands for Overview, Airway, Breathing, Circulation, Disability, and Exposure (Table 1). The following pages are a short description of the O-ABCDE approach. For more in-depth knowledge, the reader is referred to the ATLS course book (Committee on Trauma 2018) as well as to the *Advanced Medical Life Support* course book (National Association of Emergency Medical Technicians 2019).

2.1 Overview

When approaching an acutely ill patient, it is of vital importance to recognise or exclude a cardiac arrest. If the patient is awake and alert, it is an easy task to exclude cardiac arrest. That is also the case if the patient is standing or sitting up, and talking. To assess whether an unconscious patient has cardiac arrest, the patients breathing must be evaluated. If the patient is breathing, cardiac arrest can be excluded, and the physician can move on to "Airway". If the patient, however, is not breathing or has an agonal respiration,[2] a cardiac arrest must be recognised, and cardiopulmonary resuscitation (CPR) immediately started. The European Resuscitation Council does not recommend pulse check since it has been shown that it is difficult to identify a peripheral pulse during an emergency (Olasveengen et al. 2021).

[1] One of the important sources of medical errors is believed to be cognitive bias of which premature closure is one of them. Premature closure is an error where the treating physician prematurely recognises a diagnosis, failing to consider other – maybe more dangerous – diagnosis.

[2] Agonal respiration is gasping in an unconscious individual in cardiac arrest and is not to be confused with regular breathing as this gasping is not sufficient for ventilation (in't Veld and Hirshon 2020). Agonal respiration is believed to be a brain stem reflex caused by deprived blood flow to the brain stem (Eisenberg 2006).

Table 1 The O-ABCDE approach: Assessment and treatment

Approach	Assessment	Treatment
Overview	Is the patient breathing? Has the patient a cardiac arrest?	CPR
Airway	Listen after breathing sounds Inspect the face, head/neck, mouth, and throat	CPR Magill forcep Suction Chin lift and jaw thrust OPA NPA
Breathing	Inspect thorax for injuries and asymmetry Auscultate the lungs Measure respiratory rate and blood oxygen saturation	Administration of oxygen Chest tube
Circulation	Inspect the skin colour Auscultate the heart and the abdomen Palpate the abdomen Palpate pulses Measure the capillary refill time Measure blood pressure Order a blood gas If needed, order an ECG	Fluid resuscitation, inclusive blood Administration of oxygen Administration of antibiotics Chest tube Thrombolysis
Disability	GCS assessment Pupillary reaction Sensory response upper and lower extremities Motoric response upper and lower extremities Measure blood glucose level	Administration of glucose Administration of antidote for possible intoxication
Exposure	Examine the patients front and back Measure the temperature If needed, order blood-, nasopharyngeal- and urine cultures	Attend to possible injuries Administration of antibiotics

CPR cardiopulmonary resuscitation, *OPA* oropharyngeal airway, *NPA* nasopharyngeal airway, *ECG* electrocardiogram, *GCS* Glasgow Coma Scale

2.2 Airway

The assessment of the airway is twofold: hearing for breathing sounds and inspecting the face and the head/neck as well as inspecting the mouth and throat.

A normal breathing sound excludes any significant issues with the airways. The pathological breathing sounds to focus on are stridor and snoring. The absent of breathing sounds should be interpreted as a cardiac arrest and CPR started.

Stridor is a high-pitched, continuous, and monophonic sound which indicates a partial obstruction of the upper airways. It is of vital importance to exclude that a foreign object is aspirated by looking into the patient's mouth and throat. Any foreign bodies must be removed, and for this procedure, a Magill forcep can be used if the patient is unconscious.

A snoring breathing sound is another sign of partial airway obstruction. This is often seen in the unconscious patient who is unable to keep a free airway as the tongue occludes the oropharynx (in't Veld and Hirshon 2020). Basic airway management which consists of four different procedures can in the acute setting solve the problem: chin lift, jaw thrust, oropharyngeal airway (OPA), and nasopharyngeal airway (NPA). Chin lift and jaw thrust are both a manoeuvre to open the airways of the unconscious patient. Both OPA and NPA can be used alone or in conjunction with a chin lift or jaw thrust to keep the airway of the patient open and free (Carlson and Wang 2020).

Inspection of the face and the head/neck is of importance to exclude major injuries which may cause a potential danger for the airway. For this reason, it is also important to inspect inside the mouth/throat and look for blood and vomit. The use of a suction devise is highly effective to clean inside the mouth and throat if needed. Also, when inspecting the head and the mouth, an assessment must be done with respect to cyanosis of the lips which may indicate hypoxemia (McMullen and Patrick 2013).

2.3 Breathing

When assessing the breathing of the patient, the focus is on inspection and auscultation. The assessment starts by undressing the patient and inspecting the thorax looking for injuries and whether the thorax is moving symmetrically. Respiratory rate as well as blood oxygen saturation must be measured. The patient's breathing is also observed with respect to dyspnoea and tachypnoea. Any pathological findings during this stage are treated by administrating oxygen in appropriate amount. Studies have shown that hyperoxemia may cause adverse cardiovascular effects (Neill 1969; Milone et al. 1999; Bak et al. 2007) why the amount of oxygen delivered to the ill patient should be monitored and oxygen treatment terminated when the blood oxygen saturation is ≥96% (Siemieniuk et al. 2018).

The thorax not moving symmetrically may indicate pneumothorax. How prompt the pneumothorax should be treated is based on the patient's haemodynamic stability or rather instability. A chest tube should be inserted if the patient has significant breathing difficulties or is haemodynamically instable.

There are also other life-threatening conditions which may cause significant breathing problems in need of prompt treatment. Some of these conditions are pulmonary embolism, pulmonary oedema, and haemothorax. Whether these conditions should be treated rapidly during the ABCDE approach or attended to after the first evaluation of the patient is dependent on the patient's vital parameters and general condition.

Auscultation of the lungs has an important role in the ABCDE approach. Diminished or absent lung sounds may indicate pneumothorax, haemothorax, or significant pleural effusion. Other sounds indicating pathology are rhonchus, crackle, and wheezing. Rhonchi are continuous low-pitched sounds which may indicate

pneumonia and bronchitis, wheezes are continuous high-pitched sounds indicative of asthma or chronic obstructive pulmonary disease, and crackles are discontinuous low- or high-pitched sounds suggesting heart failure or pneumonia (Kim et al. 2021).

2.4 Circulation

In this stage, the patient is assessed via inspection, auscultation, and palpation. During inspection, the patients skin colour is observed (are there any cyanosis indicating hypoxemia? Is the patient pale indicating blood loss?). The heart and the abdomen should be auscultated to exclude or recognise cardiac murmurs and bowel sounds, respectively. The abdomen should then be palpated to recognise possible tenderness and peritonitis. At least the radial pulses should also be palpated to evaluate regularity, rate, and strength. Previously, the ATLS correlated the radial, carotid, and femoral pulses to a specified systolic blood pressure. These estimations have however showed to be incorrect as these previous recommendations overestimated the systolic blood pressure (Poulton 1988; Deakin and Low 2000). The ATLS no longer recommend this approach. Instead, together with other vital parameters, for example, blood pressure and pulse, the capillary refill time[3] can be used to assess the adequacy of circulation. A capillary refill time of over 2–3 s is indicative of impaired circulation and thus shock (Nicks and Gaillard 2020). Make sure that the patient has intravenous cannulation, and if not possible, an intraosseous access must be secured.

During "Circulation", it is of significant value to obtain both an electrocardiogram (ECG) as well as an arterial or venous blood gas. While ECG can help the physician in excluding some serious heart conditions like arrhythmia, a blood gas will provide vital information in assessing how ill the patient is. Besides providing essential data with regard to the acid-base status, a blood gas also shows the rate of lactate which can be used to determine the seriousness of a patient's condition (Nicks and Gaillard 2020). A rise in the lactate level of the blood has been shown to correlate with mortality in patients being admitted to the hospital in an acute setting (Kruse et al. 2011).

Several medical conditions can cause a "C" problem, and the treatment should be symptomatic at the same time as the underlying cause or causes are identified and treated. Because of its high mortality rate, the most feared condition is shock. It is therefore imperative to not only identify this condition as soon as possible but to also start treatment promptly (Sebat et al. 2007). Shock is effectively divided into four different categories (Table 2): hypovolemic shock, obstructive shock, cardiogenic shock, and distributive shock (Mokhtari and Dryver 2015).

[3] Capillary refill time is defined as the amount of time it takes for the capillary to return to its primary colour after that it has been paled because of applied pressure to the capillary by the fingers of the examiner (Pickard et al. 2011).

Table 2 Categories of shock and their aetiology as well as pathology

Category	Aetiology	Pathology
Distributive shock	Sepsis Anaphylaxis Neurogenic	A systemic vasodilatation causes a substantial loss of intravascular volume which is distributed. This contributes to a decreased preload and SVR
Hypovolemic shock	Haemorrhagic Fluid depletion (inadequate intake) Fluid loss (vomiting and diarrhoea)	A decrease in intravascular volume causes a decrease in preload and CO, which causes a fall in the BP. A compensatory increase in SVR can be seen
Cardiogenic shock	Myocardial infarction Arrhythmia Valvular abnormality Pericardial disorder	A diminished myocardial contractility contributes to a reduced cardiac output and thus decreased BP. Compensatory increase in SVR aims to direct the blood flow to the heart and the brain
Obstructive shock	Pulmonary embolism Cardiac tamponade Tension pneumothorax	Primary because of a decrease in venous return, a decrease in preload and CO are observed contributing to a diminished BP. SVR is compensatory elevated

The table is completed with inspiration from several different references (Vahdatpour et al. 2019; Nicks and Gaillard 2020; Hussain et al. 2021; Kletecka and Benes 2021)
SVR systemic vascular resistance, *CO* cardiac output, *BP* blood pressure

Distribute shock is the most frequent type of shock at the ED (33–50%), and its most common cause is sepsis (Nicks and Gaillard 2020; Hussain et al. 2021). The most important treatment in this type of shock is fluid therapy in order to haemodynamically stable the patient. The patient should always, also, be treated symptomatically. If, for example, the blood oxygen saturation is low and the patient has a high respiratory rate, oxygen must be administrated (Puskarich and Jones 2020).

Hypovolemic shock is also a frequent type of shock at the ED (31–36%) and is caused by a loss of volume (Nicks and Gaillard 2020). In medically ill nontraumatic patients, this volume depletion is often a result of either gastrointestinal losses (e.g. vomiting and diarrhoea) or haemorrhage (e.g. gastrointestinal haemorrhage). The treatment should be focused on restoring the loss of volume why fluid or blood should be administrated (Kletecka and Benes 2021). The underlying cause should also be investigated and treated. Is, for example, the vomiting and diarrhoea because of an infection, and should antibiotics be administrated?

Cardiogenic shock is the third most frequent type of shock seen at the ED (14–29%) and is foremost caused by a myocardial infarction and arrhythmias (Nicks and Gaillard 2020). Since acute coronary syndrome and specifically ST elevation myocardial infarction is the most common aetiology of cardiogenic

shock, an electrocardiogram is imperative for the recognition of this condition (Vahdatpour et al. 2019). Besides symptomatic treatment, the most important intervention is acute revascularisation.

Obstructive shock at the ED is rare (1%) and caused by pulmonary embolism, cardiac tamponade, or tension pneumothorax (Nicks and Gaillard 2020). The most common signs of obstructive shock are dyspnoea as well as jugular venous distension which often is identified already during "Airway" (Kim 2018). Because of the difficulty in diagnosing obstructive shock, and since the aetiologies of that shock have resembling symptoms like chest pain and dyspnoea, a thorough medical history and examination is vital. Both tension pneumothorax and cardiac tamponade can present with jugular venous distention. The former may also have a tracheal deviation which can be helpful during differential diagnosis. Patients with pulmonary embolism may have asymmetric swelling in the lower extremities (Abella and Bobrow 2020).

A tension pneumothorax must immediately be treated by needle decompression and insertion of a chest tube (Nicks and Manthey 2020). Treatment of a haemodynamically instable patient with cardiac tamponade or pulmonary embolism consists of fluid therapy followed by pericardiocentesis and thrombolysis, respectively (Kline 2020; Synovitz and Brown 2020).

2.5 Disability

Disability is the neurological assessment of the patient and consists of a basic neurological examination as well as an evaluation of the patient's level of consciousness. The neurological examination should be focused on bilateral pupillary reaction in addition to sensory and motor responses of the upper and lower extremities when stimulated. The level of consciousness is assessed using the Glasgow Coma Scale.

There are several potentially life-threatening conditions which can cause a "D" problem. Some of the most important conditions to recognise during this phase are hypoglycaemia, intoxication, and stroke.

Hypoglycaemia often mimics stroke thus an objective assessment by obtaining a blood glucose level is of high importance. If the patient is hypoglycaemic, glucose must be administrated. Stroke is often diagnosed based on patient history and a thorough neurological examination. The latter is of high value since stroke can present with subtle symptoms. Stroke can be caused by an embolus or thrombosis (approximately 87% of all stroke cases) and is therefore called ischaemic stroke. The other type of stroke, which is less frequent (approximately 13% of all stroke cases), is haemorrhagic stroke (Go 2020). Prompt brain imaging, preferably computed tomography (CT), is therefore imperative to exclude haemorrhagic stroke which has a different management than an ischaemic stroke.

Intentional and unintentional intoxication is a frequent condition seen at the ED. Patient history is important to assess possible psychiatric ill health and medical records. Since an intoxication may be unintentional, the patient's medical records

may, for example, reveal that the patient is prescribed opioids or benzodiazepines thus giving clues on possible aetiology of the intoxication. The patient history including possible prescribed medications, together with the patients toxidrome,[4] can guide the physician towards the correct identification of the intoxicated agent.

An ECG and blood gas is vital to assess. Some substances may have serious cardiologic impact which an ECG can identify (Greene 2020). Most important in assessing the ECG is to analyse the rhythm, QRS interval,[5] and the QTc interval[6] (Stenskilsson and Dryver 2011). With a blood gas, glucose, electrolytes, and the patient's respiration can be assessed. Any electrolyte imbalance should be treated. A respiratory acidosis should be treated by ventilating the patient (Stenskilsson and Dryver 2011). If the patient has a metabolic disturbance, the anion gap[7] should be quantified which can assist the physician with differential diagnosis (Kelen and Cline 2020).

There are several available antidotes for different substances. It is, however, seldom that any antidotes are needed before the physician has concluded his/her ABCDE. Some antidotes though may be vital already during the "Airway" and "Breathing" assessments if the patient has difficulties maintaining free airway or problems with respiration like low respiratory rate. Two such antidotes are naloxone which is used for suspected opioid intoxication and flumazenil which is indicated when suspecting intoxication with benzodiazepines (Greene 2020).

2.6 Exposure

The last phase of the ABCDE approach is "Exposure". The whole body of the patient is to be assessed during this phase. Expose the skin. Are there any signs of trauma? Rashes? Bleeding? Both the patients front and back must be thoroughly examined. Attend to any possible injuries.

A temperature is also required during this phase. If the patient is hypothermic, apply warm blankets and fluid (Brown 2020). A fever can indicate a serious infection thus guiding the physician to a correct diagnosis. Do not forget to prescribe blood, nasopharyngeal, and urine cultures before the administration of antibiotics.

[4] The set of symptoms of a substance causing an intoxication is referred to as a toxidrome.

[5] Also known as the QRS duration is measured from the beginning of the Q wave to the end of the S wave and is to be $\leq$0.10 s.

[6] QTc is short for corrected QT interval. A prolonged QTc is associated with an increased risk of malignant arrhythmias. Because the QT interval is related to the heart rate, the QTc improves the identification of such patients. A normal QTc is defined as $\leq$0.44 s and $\leq$0.46 for males and females, respectively (McGuinness et al. 2007).

[7] Anion gap is used to assess metabolic acidosis and is quantified via this formula: $Na^+ - \left(Cl^- + HCO_3^-\right)$. A normal anion gap is defined as 6–12 mEq/L.

Table 3 Oncologic emergencies discussed in this chapter

Metabolic emergencies
Hypercalcaemia
Hyponatraemia
Tumour lysis syndrome
Hematologic emergencies
Disseminated intravascular coagulation
Neutropenic fever
Cardiovascular emergencies
Malignant pericardial effusion and cardiac tamponade
Superior vena cava syndrome
Venous thromboembolism
Neurologic emergencies
Increased intracranial pressure
Malignant spinal cord compression
Treatment-related emergencies
Immune-related adverse events caused by immune checkpoint inhibitors

3 Oncologic Emergencies

Oncologic emergencies are a series of potentially life-threatening conditions which can manifest over hours or months and years. These emergencies can be categorised and organised in different ways, based on, for example, the symptoms they can cause or based on their anatomical and physiological pathologies. For simplicity, oncological emergencies in this chapter have been classified into five different categories, all of them containing at least one condition: metabolic, haematologic, cardiovascular, neurologic, as well as treatment related (Table 3). The conditions are chosen based on their challenging diagnosis or treatment and will be discussed with respect to pathophysiology, clinical presentation, diagnosis, and treatment.

As oncologic emergency patient's primary seeks the ED because of their severe symptoms (Klemencic and Perkins 2019), the selected conditions will be discussed as if the patient is at the emergency room of the ED in an unstable condition. Thus, only acute treatment during the initial assessment and before other consultants are contacted are discussed.

3.1 Metabolic Oncologic Emergencies

3.1.1 Hypercalcaemia

With an incidence of 10–30%, hypercalcaemia is the most common metabolic oncologic emergency (Stewart 2005). The condition is associated with most type of cancers and is defined as a total serum calcium (Ca^{2+}) concentration above 10 mg/dL (2.5 mmol/L) or above 5.6 mg/dL (1.4 mmol/L) if measuring ionised calcium

(Wagner and Arora 2017). The Common Terminology Criteria for Adverse Events defines severe hypercalcaemia as a corrected serum calcium of more than 13.5 mg/dL (3.4 mmol/L) or an ionised calcium of above 7.2 mg/dL (1.8 mmol/L) (National Cancer Institute 2017).

Pathophysiology There are four pathways to develop hypercalcaemia. In approximately 80% of the cases, the cause of the hypercalcaemia is humoral (Klemencic and Perkins 2019), followed by local osteolytic activity in nearly 20% of the cases (Higdon et al. 2018). The remaining two pathways, 1,25-dihydroxyvitamin D-mediated hypercalcaemia as well as ectopic hyper parathyroidism, are highly rare and account for under 1% of the causes behind cancer-related hypercalcaemia (Stewart 2005; Rothberg et al. 2022).

The humoral pathway is characterised by the tumoral secretion of parathyroid hormone-related protein shortened PTHrP. The PTHrP affects the bone and the kidneys, contributing to an increased osteoclastic activity and an increased reabsorption of calcium in the renal tubules, respectively (Guise and Wysolmerski 2022). The local osteolytic activity occurs in patients with skeletal metastases which produce cytokines that increase the activity of the osteoclasts. Hypercalcaemia occurs as calcium is flooded into the blood stream because of the osteoclastic activity and exceeds the rate of calcium which the kidneys can eliminate (Guise and Wysolmerski 2022).

Clinical Presentation Hypercalcaemia affects several different anatomical and physiological systems. The symptoms may therefore be nonspecific why the diagnosis may be missed at the initial assessment (Strijbos and Punie 2016; Wagner and Arora 2017). The clinical manifestation is related to the rate of calcium in the blood and how rapid the condition has developed and may consists of, among others, nausea and vomiting, constipation, lethargy, anorexia, polyuria, polydipsia, as well as confusion (Halfdanarson et al. 2006; Pi et al. 2016; Higdon et al. 2018; Klemencic and Perkins 2019). The European Society for Medical Oncology also mentions abdominal pain as a symptom of hypercalcaemia caused by constipation, pancreatitis, or peptic ulcer (Strijbos and Punie 2016).

Diagnosis The only way to diagnose hypercalcaemia is via a blood test where ionised serum calcium or total serum calcium is measured. While ionised serum calcium is the most reliable test (Lewis et al. 2011), many still measures total serum calcium. As close to half of the calcium in the blood is albumin bound, it is important to measure total serum calcium with respect to serum albumin[8] if the patient also has hypoalbuminaemia (Pi et al. 2016; Klemencic and Perkins 2019).

[8] Corrected calcium mg/dL = Total serum calcium mg/dL + 0.8 (4.0 – serum albumin g/dL)
Corrected calcium mmol/L = Total serum calcium mmol/L + 0.02 (40 – serum albumin g/L)

An ECG is of importance since it has been shown that hypercalcaemia can cause ECG changes and cause arrhythmias (Ahmed and Hashiba 1988; Diercks et al. 2004). One recent study from France, however, could show that hypercalcaemia, defined as a total serum calcium >4 mmol/L equal to 16 mg/dL, at their ED, did not cause any life-threatening arrhythmias (Guimard et al. 2018). An ECG should though always be ordered as the patient may have other accompanying electrolyte disturbances adversely affecting the heart.

Treatment Because of their symptoms, hypercalcaemia patients are often highly dehydrated which also causes reduced renal filtration which in turn exacerbates the hypercalcaemia as the rate of calcium filtration decreases (Guise and Wysolmerski 2022). Fluid therapy using isotonic fluid (0.9% NaCl) should therefore be administrated as soon as possible (Pi et al. 2016; Wagner and Arora 2017). How much and how fast the fluid should be administrated is dependent on the severity of the patient's hypercalcaemia and her symptoms (Guise and Wysolmerski 2022), but as much as 1000–2000 ml as a bolus may be needed if the patient is severely dehydrated (Klemencic and Perkins 2019).

Since rehydration is the most important objective at the ED, other treatments than fluid therapy is often not necessary (Wagner and Arora 2017). In patients with severe hypercalcaemia, however, in addition to fluid therapy, also treatment with calcitonin as well as zoledronic acid can be administrated already at the ED if the patient because of different reasons cannot be promptly admitted to the intensive care unit. Calcitonin lowers the blood calcium by partly inhibiting osteoclasts thus reducing bone resorption and partly by increasing renal elimination of calcium (Davey and Findlay 2013). It can be dosed as 4 units/kg intramuscular or subcutaneous, and its effect can be seen after 3–6 h. Zoledronic acid, a bisphosphonate, is specifically indicated for cancer-related hypercalcaemia. It affects the bone tissue inhibiting osteoclasts. It can take between 2 and 4 days for their maximum effect (Shane and Berenson 2022). Zoledronic acid is administrated intravenously at a dose of 4 mg.

3.1.2 Hyponatraemia

The incidence of hyponatraemia in hospitalised cancer patients has been shown to be as high as 47% and is associated with a poor prognosis (Doshi et al. 2012). Hyponatraemia is defined as a concentration of sodium (Na^+) <135 mmol/L and is classified as mild (130–135 mmol/L), moderate (125–129 mmol/L), and profound (<125 mmol/L) (Spasovski et al. 2014).

Pathophysiology Both the cancer disease and its treatment can cause hyponatraemia. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is the primary cause of hyponatraemia in cancer patients and is caused by tumours producing vasopressin[9] (Spring and Munshi 2021). The excessive

[9]Vasopressin is produced in the hypothalamus and is also called antidiuretic hormone (ADH) or arginine vasopressin (AVP).

production of vasopressin contributes to a higher degree of anti-diuresis thus causing water reabsorption which in turn leads to a decreased plasma osmolality (i.e. hyponatraemia) (Miller 2001). With respect to cancer treatment, chemotherapy has shown to cause hyponatraemia by either affecting paraventricular and supraoptic neurons or causing injuries to the renal tubules which in turn contributes to an impaired water and electrolyte balance (Yeung 2021).

Clinical Presentation Severity of symptoms is correlated to partly the rate of sodium concentration in the blood and partly on how fast the hyponatraemia has developed. The Clinical Practice Guideline on Diagnosis and Treatment of Hyponatraemia defines severe symptoms as vomiting, cardiorespiratory distress, abnormal and deep somnolence, seizures, and coma (Spasovski et al. 2014).

Diagnosis Blood test showing sodium concentration is the only way to diagnose hyponatraemia.

Treatment Hyponatraemic patients with symptoms, irrespective of the blood sodium concentration and whether it is acute or chronic, must be treated rapidly and aimed at countering cerebral oedema. There are two different guidelines on the treatment of severe hyponatraemia, and both recommend treatment with intravenous hypertonic fluid (3% NaCl). Clinical Practice Guideline on Diagnosis and Treatment of Hyponatraemia recommends the following treatment: administer 150 ml intravenous hypertonic fluid (3% NaCl) over a period of 20 min. While evaluating the blood sodium concentration via a blood test, and administer a second 150 ml intravenous 3% NaCl. This treatment can be repeated until a blood sodium concentration increase of 5 mmol/L is accomplished (Spasovski et al. 2014).

The other guideline, the Expert Panel Recommendations, suggests intravenous administration of 100 ml of 3% NaCl over a period of 10 min which can be repeated two additional times. The aim of this regimen is to increase the blood sodium concentration by between 4 and 6 mmol/L (Verbalis et al. 2013).

3.1.3 Tumour Lysis Syndrome

Tumour lysis syndrome (TLS) is foremost associated with hematologic malignancies but can also occur in patients with solid tumours (Higdon et al. 2018; Brydges and Brydges 2021). Even though it is a rare condition involving between 3% and 6% of patients with haematological cancers (Punie and Strijbos 2016), TLS has a high mortality rate of between 29% and 79% (Klemencic and Perkins 2019). Because of its significant mortality, it is of vital importance to identify the condition rapidly and initiate treatment.

Pathophysiology TLS is foremost caused by cancer treatment like chemotherapy, immunotherapy, and glucocorticoids (Brydges and Brydges 2021) but can also happen spontaneously (Wesemüller and Taverna 2020).

Table 4 Clinical signs and symptoms of tumour lysis syndrome

Nausea
Vomiting
Somnolence
Haematuria
Flank pain
Oliguria/anuria
Oedema and fluid overload with hypertension
Azotaemia
Acidosis
Congestive heart failure
Muscle cramps
Tetany
Syncope
Seizures
Sudden death

TLS can occur between 6 h and 72 h after the initiation of the treatment and is caused by tumour cell lysis which in turn releases elements of the cell – potassium, phosphate, uric acid, nucleic acid – into the blood stream causing hyperuricaemia, hyperkalaemia, and hyperphosphatemia (Davidson et al. 2004; Punie and Strijbos 2016; Thandra et al. 2020; Brydges and Brydges 2021). The hyperuricaemia causes acute renal impairment because of urate crystal formation causing obstructions in the tubules but also by causing vasoconstriction contributing to diminished renal blood flow (Punie and Strijbos 2016; Thandra et al. 2020). Hyperkalaemia can cause malignant arrhythmias as well as severe neuromuscular symptoms which are caused by depolarisation of cells increasing myocardial and neuronal excitability (Hunter and Bailey 2019). Hyperphosphatemia causes two main problems: kidney injury by depositing in the tubules as calcium phosphate crystals as well as hypocalcaemia because phosphorus binds calcium (Thandra et al. 2020).

Clinical Presentation The symptoms of TLS are directly related to the electrolyte disturbance as well as the acute kidney injury why the patient can present with a variety of clinical signs. Table 4 presents the symptoms identified by the European Society for Medical Oncology (Punie and Strijbos 2016).

Diagnosis The diagnosis is based on three pillars: anamnesis (the patient has a malignancy and has most likely been recently treated with an agent), clinical symptoms (Table 4), and laboratory pathology (hyperuricaemia, hyperkalaemia, hyperphosphatemia, hypocalcaemia, increased creatinine level). Cairo and Bishop (2004) propose that for TLS to be diagnosed, the patient must have laboratory pathologies as well as one of the three following clinical signs: renal insufficiency, cardiac arrhythmias/sudden death, and/or seizures. Because of this, an ECG is vital.

Treatment The most important treatment is fluid therapy and managing the electrolyte abnormalities. Fluid therapy should be conducted by administrating intravenous crystalloid fluid at a rate of >100 ml/h in order to increase urinary output (Ostermann et al. 2019).

Of vital importance is to treat hyperkalaemia which is the most serious and life threatening symptom of TLS (McCurdy and Shanholtz 2012; Pi et al. 2016). If the patient has symptoms (muscle weakness/paralysis or cardiac conduction abnormalities/arrhythmias) or a blood potassium concentration of >6.5 mEq/l (>6.5 mmol/L), acute treatment must be initiated: intravenous calcium gluconate (10 mL of 10% solution) or calcium chloride (500–1000 mg) over a period of 2–3 min to reduce the risk of malignant arrhythmias, and 10 units of rapid-acting insulin in order to rapidly shift potassium intracellularly. Observe that glucose should be administrated simultaneously if the patient's blood glucose level is <250 mg/dL (<13.9 mmol/L) (Mount 2022).

3.2 Haematologic Oncologic Emergencies

3.2.1 Disseminated Intravascular Coagulation

The incidence of disseminated intravascular coagulation (DIC) in cancer patients with solid tumours have been shown to be between 7% and 15%, while the same figure for haematological malignancies is between 15% and 20% (Pi et al. 2016; Levi 2019). The condition is seen foremost in patients with leukaemia, specifically acute promyelocytic leukaemia (Adelborg et al. 2021).

Pathophysiology It is believed that malignant cells express tissue factor (TF) which contributes to an activation of systemic coagulation cascade causing a significant disparity between the coagulation and anticoagulation pathways. This imbalance causes consumption of coagulation factors like among other platelets, fibrinogen, as well as prothrombin (Martinelli et al. 2016; Pi et al. 2016; Levi 2019). The activation of the coagulation system causes fibrin formation contributing to the increase of plasmin and thus fibrinolysis which is associated with cancer-related DIC (Adelborg et al. 2021).

Clinical signs and symptoms of DIC are highly related to the pathophysiology described. The activation of the coagulation cascade develops clots which block vessels thus contributing to ischaemia and consequently organ failure. At the same time, the fibrinolysis will contribute to haemorrhage which cannot be controlled because of consumption of coagulation products and factors (Martinelli et al. 2016; Pi et al. 2016; Adelborg et al. 2021).

Both radiotherapy as well as chemotherapy is also believed to cause DIC, as these treatments disrupt the endothelial cells (Levi 2019).

Clinical Presentation In the acute setting, the most significant symptoms are haemorrhage and thrombose formation (i.e. venous thromboembolism) either alone or in combination (Levi 2019). According to the European Society for Medical Oncology, the haemorrhage manifests itself from at least three different sites – ears, nose, and throat, gastrointestinal tract, respiratory tract, site of venepuncture or intravenous infusion (Martinelli et al. 2016).

Diagnosis The diagnosis of DIC should be made analysing the patient's anamnesis, clinical signs and symptoms, as well as the ordered blood tests (e.g. prothrombin time (PT), activated partial thromboplastin (aPTT), platelets). Leung (2022) argues that in order to diagnose established acute DIC, the patient must have laboratory pathologies: reduced platelet count, prolonged PT and aPTT, low fibrinogen, and increased D-dimer. One problem, however, is that most of these tests are not available during the acute initial management of the critically ill patient at the ED. Anamnesis and clinical signs and symptoms are therefore the most important tools in suspecting DIC.

Treatment The treatment should initially be symptomatic and in accordance with the ABCDE approach presented above. Thrombosis can be treated with different anticoagulants based on local guidelines. Haemorrhage can be treated by blood transfusion, administrating tranexamic acid, platelet transfusion if platelet count is $<10 \times 10^9$/L, or in case of severe haemorrhage, transfusion of fresh frozen plasma should be considered (Adelborg et al. 2021; Leung 2022).

3.2.2 Neutropenic Fever

As high as 50% of patients with solid tumours and over 80% of patients with haematological cancers receiving chemotherapy will develop neutropenic fever (NF) (Alonso and Corral 2016). Usually, NF occurs between 5 and 10 days after the chemotherapy (Lewis et al. 2011). A patient with NF presenting at the ED is often not in a critical condition in need of rapid emergency care. However, patients with NF have a higher risk of developing sepsis and septic shock which has a mortality rate of up to 50% (Klemencic and Perkins 2019; Long and Koyfman 2019). These patients need urgent emergency medical care.

Pathophysiology Even though the most common cause of NF is chemotherapy, other aetiologies are disruption of haematopoiesis either because of haematologic malignancies or a tumour infiltrating the bone marrow (Thandra et al. 2020). In all cases, the bone marrow will be damaged resulting in depressed bone marrow function and thus neutropenia (Long and Koyfman 2019).

Because of the neutropenia, the immune system is compromised and more prone to infections. Bacterial and fungal infections are the most common causes of NF, but a culprit can only be identified in approximately one-third of the cases (Courtney et al. 2007; Alonso and Corral 2016; Klemencic and Perkins 2019). It is primary gram-positive bacteria which causes NF (Alonso and Corral 2016; Klemencic and Perkins 2019).

Clinical Presentation Critically ill NF patients present with symptoms of sepsis and septic shock which include fever, hypotension, tachycardia, altered mental status, increased respiratory rate, as well as altered level of consciousness (Puskarich and Jones 2020).

Diagnosis NF patients present with fever and a low neutrophil count ($<0.5 \times 10^9$/L) (Alonso and Corral 2016). At the ED, however, it will take time before a neutrophil count can be obtained. The focus should therefore be on anamnesis (i.e. cancer patient just having chemotherapy). Blood and urine cultures should be obtained. Based on the anamnesis, imaging (i.e. pulmonary X-ray or CT of the abdomen) should be considered. As sepsis is a clinical diagnosis, a patient with sepsis/septic shock is often diagnosed only based on clinical signs (e.g. hypotension) and symptoms (e.g. fever).

Treatment Septic shock must be treated aggressively with fluid (i.e. 1000–2000 ml intravenous crystalloid as a bolus). If the patient does not respond to this, vasopressors (i.e. 0.5–30 μg/min intravenous norepinephrine) must be considered (Puskarich and Jones 2020). Another important pillar of the septic shock treatment is antibiotics. As the microorganism causing the shock is often unknown, a broad-spectrum antibiotic in accordance with local guidelines should be intravenously administrated (Higdon et al. 2018; Klemencic and Perkins 2019).

3.3 Cardiovascular Oncologic Emergencies

3.3.1 Malignant Pericardial Effusion and Cardiac Tamponade

The heart is encircled by a double-layered sac, the pericardium. In adults, there are 20–60 mL of fluid between the layers acting as lubricant (Vogiatzidis et al. 2015). Any increase in the normal amount of pericardial fluid is defined as a pericardial effusion, and cardiac tamponade occurs when the effusion continues to increase thus impairing cardiac function (Hoit 2022). Both pericardial effusion and cardiac tamponade can be caused by a variety of aetiologies, malignancy being one of them. Up to one-third of cancer patients have shown to have malignant pericardial effusion (McCurdy and Shanholtz 2012; Higdon et al. 2018).

Pathophysiology Malignant pericardial effusion can develop via different pathways. The most common causes are a tumour close to the heart directly affecting the pericardium (e.g. mediastinal lymphoma) as well as metastases affecting the pericardium (e.g. non-contiguous breast cancer) (Lewis et al. 2011). Most frequent malignancy associated with the involvement of the pericardium is malignant melanoma which occurs in between 40% and 70% of the patients (Griguolo and Guarneri 2016). Other less common causes of malignant pericardial effusion are radiation- and chemotherapy (Griguolo and Guarneri 2016; Spring and Munshi 2021).

As fluid accumulates in the pericardium, the intrapericardial pressure increases contributing to the compression of the chambers. Consequently, the diastolic filling will be impaired, causing a significant reduction of the cardiac output (Reddy et al. 1990; Spodick 2003).

Clinical Presentation The clinical presentation is dependent on how fast the effusion has developed. Patients with malignancies can accumulate as much as 2000 mL of pericardial fluid before cardiac tamponade appears and the patient presents with severe symptoms (Spodick 2003).

The most serious presentation of cardiac tamponade is cardiac arrest followed by cardiogenic shock. If the latter, the patient has typical shock symptoms like tachycardia, hypotension, cyanosis, and cold skin and extremities (Manthey and Nicks 2020). Other symptoms may be chest pain, dyspnoea, pleuritic pain, and pulsus paradoxus.[10] Tachycardia and jugular venous distention are the two most important symptoms highly related to cardiac tamponade (Spodick 2003).

Diagnosis An ECG may show electrical alternation but is often normal and nonspecific (Spodick 2003; Synovitz and Brown 2020). The most important diagnostic tool with respect to the critically ill patient is ultrasound which today is common at EDs worldwide (Spodick 2003). If an ultrasound is not available and the patient is stable enough for imaging, a chest radiograph or thoracal CT should be ordered.

Treatment In the acute setting, drainage of the pericardium via pericardiocentesis is the only lifesaving option. When preparing for this, crystalloid infusion may be of importance in order to improve right ventricular volume (Synovitz and Brown 2020). Pericardiocentesis should be conducted with the use of an ultrasound to avoid injuries to the heart and other organs, but in very acute cases where imaging is not possible (i.e. patient with cardiac arrest or haemodynamically instable) or available, a blind pericardiocentesis should be performed and the needle should be inserted subxiphoid (Synovitz and Brown 2020).

3.3.2 Superior Vena Cava Syndrome

Between 73% and 93% of all cases of Superior Vena Cava Syndrome (SVCS) are caused by a malignancy with lung cancer and lymphoma being the primary causes (Halfdanarson et al. 2006; Foy and Kurup 2016).

Pathophysiology SVCS can be caused via three different routes: compression (e.g. lung tumour compressing the superior vena cava), invasion of a tumour (e.g. lung tumour or a mediastinal tumour) into the superior vena cava (SVC), and development of a thrombosis in the SVC (Foy and Kurup 2016; Spring and Munshi 2021). The consequence is diminished or total stop of blood flow which in turn causes increased venous pressure followed by interstitial oedema (Foy and Kurup 2016).

[10] A fall of >10 mmHg in systolic blood pressure during inspiration in patients with cardiac tamponade. This causes peripheral pulses to have different strengths thus the word paradoxus.

Clinical Presentation The most common symptom is facial oedema (McCurdy and Shanholtz 2012; Higdon et al. 2018). Serious symptoms of SVCS may be dyspnoea, breathing difficulties, swelling of the tongue, and stridor caused by laryngeal oedema (Foy and Kurup 2016). The elevated SVC pressure can also cause cerebral oedema thus causing headache, nausea and vomiting, altered mental status, and death because of cerebral ischaemia and herniation (Foy and Kurup 2016). Jugular vein distention and vivid superficial vascularity of the neck and upper thorax are other symptoms of SVCS (Higdon et al. 2018).

Diagnosis SVCS is a clinical diagnosis, but a CT, which is available in most EDs, can contribute to vital information like how large the tumour compressing the SVC is and where the SVC obstruction is located (Foy and Kurup 2016).

Treatment SVCS is treated symptomatically, prioritising life-threatening symptoms like obstruction of the airway. The critically ill patient is in need of emergency endovenous recanalisation where a stent is placed in the SVC or, in case of a thrombosis obstructing the vessel, thrombolysis and thrombectomy (Rothberg et al. 2022). Corticosteroids should only be used if the patient's malignancy is known and is sensitive to corticosteroids (Drews and Rabkin 2022).

3.3.3 Venous Thromboembolism

Cancer patients are predisposed to venous thromboembolism (VTE), which can be the first symptom of a malignancy. The risk for a cancer patient to develop VTE is 20%, and the VTE presents itself as pulmonary embolism (PE) or as a deep vein thrombosis (DVT) in the lower extremities (Chiramel et al. 2016). In addition to the disease itself, treatment with chemotherapy increases the risk of VTE (Levi 2019). Being the second most common cause of mortality in cancer patients, VTE is of high importance to diagnose and treat (Foy and Kurup 2016). As PE is the most feared VTE and DVT often has a benign course, the focus of this section will be on PE.

Pathophysiology There are several ways in which cancer highly increases the risk of developing VTE, and some of the pathways may be associated with specific cancer forms (Abdol Razak et al. 2018). A general pathophysiology is tumour expression of different procoagulants of which TF is the best studied. TF activates the extrinsic pathway of coagulation and the production of thrombin, thus causing blood clots. Tumours can also produce microparticles expressing TF which furthermore contributes to coagulation and formation of clots (Abdol Razak et al. 2018). VTE in cancer patients can also be caused by chemotherapy which activates endothelial cells thus resulting in several changes (e.g. increased TF expression) further increasing the risk of VTE (Chiramel et al. 2016).

Once the clot if developed, often in the lower extremities, it travels via the blood stream to the lung arteries.

Clinical Presentation A critically ill patient with PE often presents to the ED with symptoms like respiratory distress (e.g. dyspnoea), chest pain, shock (i.e. obstructive shock), and cardiac arrest (Chiramel et al. 2016; Yamamoto 2018; Rothberg et al. 2022).

Diagnosis In the responsive patient, an ECG most likely will show signs of pulmonary hypertension: tachycardia, negative T-waves in the septal and anterior leads, as well as right bundle branch block (Kline 2020). CT is the best diagnostic tool; however, in the haemodynamically instable critically ill patient, imaging is often not appropriate, why treatment should be started based on anamnesis and clinical signs and symptoms.

Treatment Shock treatment and upholding a stable ABCDE is the primary objective of the emergency care. The most urgent and effective treatment in these patients is thrombolysis (Yamamoto 2018; Kline 2020).

3.4 Neurologic Oncologic Emergencies

3.4.1 Increased Intracranial Pressure

Increased intracranial pressure (IICP) is a serious condition which can cause herniation and death (Rothberg et al. 2022). Up to 25% of terminal cancer patients have intracranial metastases which are the primary cause of IICP (Halfdanarson et al. 2006).

Pathophysiology Tumours metastases to the brain via the blood stream and close to 90% of them reside in the supratentorial part of the brain (Halfdanarson et al. 2006). Two routes contribute to the IICP: the tumours themselves as well as the oedema which is caused by damage to the blood-brain barrier (Lewis et al. 2011; Brydges and Brydges 2021).

Clinical Presentation Patients with IICP present with symptoms like headache, nausea and vomiting, focal neurological symptoms, and altered mental status (Lewis et al. 2011; Brydges and Brydges 2021). Seizure is another common symptom as close to 70% of all patients with metastases to the brain have experience this condition (Halfdanarson et al. 2006; de Mattos-Arruda and Preusser 2016).

Diagnosis While the anamneses (e.g. the patient has brain metastases) and clinical signs (e.g. altered mental status) may give indications of IICP, imaging (i.e. CT or magnetic resonance imaging, MRI) is vital to confirm the diagnoses but at the same time also exclude other differential diagnoses (i.e. brain haemorrhage).

Treatment The hypotonic patient should receive fluids (e.g. 3% NaCl 1000 mL intravenous) so that an adequate mean arterial pressure can be maintained (Brydges and Brydges 2021). Hypertonic fluid has been shown to more effective than

mannitol in treating IICP (Mortazavi et al. 2012). Corticosteroids (e.g. dexamethasone 10 mg intravenous) have been shown to decrease IICP why it should be used in the acute setting (Drappatz 2021). Seizures usually end spontaneously; if not, it should be managed using anticonvulsants, for example, benzodiazepines.

3.4.2 Malignant Spinal Cord Compression

Malignant spinal cord compression (MSCC), just after brain metastases, is the most frequent neurological impairment in cancer patients affecting up to 6% of them, and as many as 25% of cancer patients present with MSCC as the first symptom of their malignancy (Halfdanarson et al. 2006; Lewis et al. 2011; Köksoy and Urun 2016). The leading location for MSCC is the thoracic spine (60%) followed by the lumbosacral area (30%) and the cervical spine (10%) (Lewis et al. 2011).

Pathophysiology Haematogenous metastases to the vertebral body, where the tumour grow into the spinal canal compressing the cord, is the most common aetiology of MSCC (McCurdy and Shanholtz 2012; Spring and Munshi 2021). Another pathway in which the spinal cord is injured is when the tumour because of its compression obstructs the epidural venous plexus contributing to oedema of the white matter which in turn results in ischaemia (Prasad and Schiff 2005; Köksoy and Urun 2016). It is these injuries to the spinal cord which cause the symptoms the patient presents with.

Clinical Presentation The primary symptom of MSCC is back pain which is seen in more than 90% of the patients (Halfdanarson et al. 2006; Köksoy and Urun 2016). Other symptoms include motor deficit (between 60% and 86% of the patients), sensory deficit (between 40% and 90% of the patients), bladder and bowel dysfunction, as well as paralysis (Halfdanarson et al. 2006; Köksoy and Urun 2016; Rothberg et al. 2022).

Diagnosis CT or MRI should be conducted urgently and are the only way to completely diagnose MSCC (Halfdanarson et al. 2006; Köksoy and Urun 2016).

Treatment The most important treatment at the emergency department is the administration of intravenous corticosteroids (10–16 mg dexamethasone) (Halfdanarson et al. 2006; Köksoy and Urun 2016). Different studies have shown that a higher corticosteroid dose (96 mg) most likely have no additional effect and can, on the contrary, cause serious side effects (Heimdal et al. 1992; Sørensen et al. 1994; Graham et al. 2006; George et al. 2015). The most important effects of corticosteroids are to decrease inflammation and vasogenic oedema thus contributing to possible symptom relieve.

3.5 Treatment-Related Oncologic Emergencies

3.5.1 Immune-Related Adverse Events Caused by Immune Checkpoint Inhibitors

There are several different immunotherapy treatment types for cancer, for example, adoptive cell therapy, checkpoint inhibitors, cytokines, oncolytic virus therapy, monoclonal antibodies, and vaccines (Kennedy and Salama 2020; Taefehshokr et al. 2020). These immunotherapies aim to augment the patient's own immune system so that it can fight the invading cancer cells (McCune 2018). Unfortunately, all of them have side effects, which are referred to as immune-related adverse events, shortened irAEs (Waldman et al. 2020; Conroy and Naidoo 2022). These adverse events can occur at any time during the treatment and has an incidence of 80% and a mortality rate of between 0.36% and 1.23% (Wang et al. 2018; Rothberg et al. 2022).

Focus of this section will be on irAEs caused by immune checkpoint inhibitors (ICIs). Immune checkpoints are important regulators of the immune system and are critical to inhibit autoimmunity. Tumours can exploit this and by expressing immune checkpoints on the tumour itself, it avoids having the immune system attacking it. ICIs inhibit the tumours´ immune checkpoints why the tumour will be attacked by the T cells of the immune system (Pardoll 2012).

Pathophysiology The pathophysiology of irAEs is not fully addressed and several pathways are believed to cause the symptoms which the patients present with. One mechanism of irAEs may be that when inhibiting immune checkpoints, T cells may also attack the body's own tissues (Chan and Bass 2020). Other mechanisms are believed to be that the effects which ICIs have on the immune system can cause an increase in antibodies and cytokines thus causing a significant activation of the immune system increasing the risk of autoimmunity (Postow et al. 2018).

Clinical Presentation Since irAEs can affect all organs and systems of the body, the patient can present with a variety of conditions, signs, and symptoms of which several can be life-threatening. Some of them are acute abdomen, gastrointestinal bleeding, encephalopathy, respiratory insufficiency because of pneumonitis, or muscle weakness affecting respiratory muscles, myxoedema because of hypothyroidism, hyperthyroidism causing thyroid storm, electrolyte imbalance because of adrenal insufficiency, diabetes ketoacidosis, hypophysitis, nephritis, haemolytic uremic syndrome, autoimmune haemolytic anaemia, thrombotic thrombocytopenic purpura, myocarditis/pericarditis, arrhythmias, disrupted ventricular function, and pulmonary embolism (Postow et al. 2018; Thompson et al. 2020; Schneider et al. 2021).

Diagnosis Anamneses are vital to identify patients treated with ICIs. Other diagnostic measures should be focused on the symptoms which the patient presents with (e.g. if the patient has chest pain, an ECG should be obtained, and cardiac troponin should be ordered).

Treatment The treatment is symptomatic and focused on the specific organ or organs affected. Main objective of the symptomatic treatment is to stabilise the patient. One important treatment of irAEs, additional to the symptomatic treatment, is the intravenous administration of corticosteroids which acts immunosuppressive (Schneider et al. 2021).

4 Conclusion

This chapter has two main objectives: (1) describe the initial assessment and treatment of the critically ill patient based on the O-ABCDE approach and (2) provide an overview over some of the most challenging oncologic emergencies.

The O-ABCDE approach provides a systematic and methodical path to assess and treat the critically ill patient. While the main purpose of this approach is to identify the most life-threatening conditions and promptly treating them, it is of most importance to also care for other symptoms and signs which may indicate a potentially life-threatening condition.

Understanding why oncologic emergencies occur and how they can be treated is vital for anyone working with emergency medicine and emergency care. While the focus of treatment in these patients should be on stabilising the patient respiratory and haemodynamically, the responsible emergency physician must also consider other conditions which may cause the patient's signs and symptoms or coexist with the oncologic emergency.

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