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Published in:
Pediatric Neurology

DOI:
10.1016/j.pediatrneurol.2013.07.002

2013

Access to Neuropsychologic Services After Pediatric Brain Tumor

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Short title: Access to Neuropsychologic services

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Word count: Body text: 1758
Abstract: 248
Tables: 1 (No figures)

Introduction

The annual incidence of pediatric brain tumors in Sweden is 4.2 per 100,000 children (0-16 years of age) and the 10-year survival rate is approximately 72%[1]. However many pediatric brain tumor patients suffer from long-term physical and cognitive impairments[2-5] including deficits of attention, memory, tempo and executive function[6-10]. Two primary risk factors for cognitive impairments in patients with pediatric brain tumors are age at diagnosis (below 5 years) and treatment with cranial radiation therapy (CRT)[11-14]. Other identified risk include; treatment with intrathecal chemotherapy, localization and type of tumor, surgery and complications from surgery (e.g. bleeding, infection, periods of increased intracranial pressure (ICP), cerebrovascular complications and female gender[3,4,15].

With a growing body of evidence demonstrating the risk for long-term cognitive impairments in PBT survivors, in 2007 the North-American Children's Oncology Group (COG) recommended that "the developmental status of survivors, including their education and vocational progress and their general adaptive functioning, should be assessed annually by their primary health care provider."[16] In addition, COG recommended neuropsychologic follow-up for all pediatric brain tumor patients from the first-point of contact with long-term follow-up program, when starting a new school, and whenever difficulties in school or wider psychosocial functioning are observed[16]. In 2003 the Swedish Working Group for Pediatric CNS Tumors (VCTB) developed guidelines recommending neuropsychological evaluation before surgery (if possible), and at one, three and five years after diagnosis[17]. Efforts are underway to harmonize guidelines across countries but there is a general recognition that systematic assessment of neurocognitive deficits is a priority for children with cancer[18].

The Department of Pediatrics, Skåne University Hospital Lund, treats 15% of all children diagnosed with pediatric brain tumor nationwide. Neuropsychologic resources have been available at the department since 1995 but systematic neuropsychologic screening of all pediatric brain tumor patients were not carried out until 2007. The aim of this study was to investigate rates of referral for neuropsychologic examination between 1995 and 2006 and factors that may have influenced the decision to refer.

Patients and methods

Patients

Between 1993 and 2004, 152 children (0-18 years) were diagnosed with a pediatric brain tumor at the Department of Pediatrics, Skåne University Hospital Lund. Patients who died within one year of diagnosis (n=20) were excluded from our analyses because they were usually so physically ill that a neuropsychologic evaluation was simply not indicated. Thus the final sample available for analyses was 132 survivors of pediatric brain tumor. All patients living in the southern region of Sweden (with approx. 1,7 million inhabitants) are treated in this department representing 15% of the Swedish population of pediatric brain tumor patients. The types of cancer, gender ratio (slightly more boys than girls), and one-year survival rate for this regional sample was extremely similar to those reported for the country as a whole in the Swedish Childhood Cancer Registry[19]. One notable exception was that patients in the present sample had a higher percentage of astrocytomas, which may reflect the fact that patients who survived less than one year after diagnosis were excluded (n=20, 10 with medulloblastomas, 6 with pons or brainstem glioma and 4 with high grade astrocytoma, ependymoma or oligodendroglioma).

Data collected

All data were taken from the medical records at the Department of Pediatrics, Skåne University Hospital, Lund, including the additional neuropsychologic reports

available for the 64 patients who were referred for neuropsychological evaluation. The two groups of pediatric brain tumor patients (referred and non-referred patients) were compared on the following variables: age at first diagnosis, gender, treatment, classification and localization of tumor (infra-/supratentorial), size of the tumor at diagnosis (largest diameter in centimeters), death within the study period, increased ICP at diagnosis, ventriculo-peritoneal shunt or ventriculostomy, neurocutaneous syndromes (neurofibromatosis or tuberous sclerosis), medication and epilepsy (Table 1). Treatment was coded as four (non-exclusive) dichotomous variables (0 or 1): surgery, chemotherapy, CRT and whole brain radiation therapy. Tumor classification was made according to the World Health Organization's third International Classification of Childhood Cancer (ICCC-3)[20] but for the purposes of the present analyses these were recoded as either astrocytoma or non-astrocytoma. A patient was coded as having epilepsy if they had an explicit diagnosis in the medical records and the seizures were not solely the initial symptoms of a pediatric brain tumor. Medications recorded were either hormone replacement therapy or anti-epileptic drugs given at any point within the study period. The children got more medication but only these two were frequent and interesting enough.

For patients who were referred for neuropsychologic examination, they were coded as having cognitive impairment with IQ less than 70 if this diagnosis was clearly stated in the neuropsychologic report. A referred patient with IQ less than 80 and severely disabling learning difficulties was coded as having cognitive impairment with IQ less than 80. For patients who were not referred (i.e. only the medical records were available for inspection), available data on cognitive ability was extremely limited and type of schooling was used as a proxy where appropriate. In Sweden there are two main types of compulsory schools, one for children of normal ability and one for children with a diagnosis of cognitive impairment with IQ less than 70. Pediatric brain tumor patients

who were not referred for neuropsychologic examination were coded as having cognitive impairment if their medical records indicated that the child had previously been assessed and found to have an IQ less than 70 and/or they attended a compulsory school for children with such learning disabilities. Patients who had been considered for the compulsory school for learning disabilities, but who had not attended were coded as having cognitive impairment with an IQ less than 80.

Statistical methods

All statistical comparisons were carried out using IBM SPSS 20.0[21]. Differences between referred and not referred patient were assessed with t-test for continuous variables and λ^2-test for categorical variables.

Results

Approximately half of the diagnosed patients (n=64) were referred for neuropsychologic examination during the inclusion period (1995-2006). Patients were referred mostly by their pediatric neurologist. The main reason for referral was that a parent, teacher or member of the medical team observed what appeared to be significant cognitive impairments. Patients were also referred when the child was at high risk of cognitive deficits owing to the nature of their cancer treatment (i.e. CRT) or age at diagnosis (i.e., below 5 years of age).

Pediatric brain tumor patients who were referred for neuropsychologic examination were significantly more likely to have suffered from larger tumors, increased ICP at the time of diagnosis, and recurrences of their cancer (see Table 1). No other significant differences were observed between the two groups. Of note, the two groups did not differ on a range of potential risk factors for cognitive impairment (age at diagnosis, treatment type) suggesting that these factors played may have played a lesser role in the decision to refer. In addition 15 of the 68 non-referred patients (22%) contained

references in their medical records to either an IQ below 80 and/or referral to or attendance at a compulsory special education school.

Discussion

The present study was undertaken to identify the rate of referral to neuropsychologic services in a representative sample of children with pediatric brain tumors, and to identify differences between referred and non-referred patients. Consistent with the literature on risk for cognitive impairment following a diagnosis of pediatric brain tumor, patients in the referred group had larger tumors at diagnosis, increased ICP, and more relapses of cancer prior to referral. However a significant proportion of patients who were not referred also had risk factors for cognitive impairment around the time of their diagnosis or following treatment of pediatric brain tumors. For example 10% of patients in the non-referred group had whole brain radiation therapy and 41% had locally administered CRT. In addition 22% of the non-referred patients in this non-referred group had intellectual impairment with an IQ less than 80 in their medical records. At the time these patients were treated for cancer, only a few pediatric cancer centers in Sweden had access to neuropsychologic services and none of these services had the resources to screen all pediatric brain tumor patients or indeed to offer remedial treatment for those who were referred which may have influenced the observed referral rate. It is also possible that a referral was not necessary for pediatric brain tumor survivors who were already enrolled in compulsory special education.

This is the first study to evaluate referral practices with pediatric brain tumor survivors. Nevertheless our findings are in keeping with the results of a larger Swedish study of 526 adult survivors of central nervous system tumors and 550 of their parents [22]. In that study, Hovén et al. found that 41% of those who indicated that they had a health care need, reported that their needs went unmet, especially in the psychosocial services

domain. One of the most frequent specific unmet health care needs was requests from patients and parents for counseling regarding educational or behavioral problems. Thus the present study adds to a growing body of literature indicating that access to neuropsychologic services is a priority for cancer survivors and particularly those with pediatric brain tumors.

As suggested by international guidelines on the care of pediatric brain tumors, making neuropsychologic services available to every pediatric brain tumor patient is likely to improve long-term outcomes. Greater efforts are needed to disseminate these guidelines and insure compliance. In addition, data collected from systematic neuropsychologic assessments of cancer survivors should be placed in national registries in order to help evaluate the long-term effects of various treatment protocols, as newer treatments are emerging that are designed to spare normal brain tissues from radiation (e.g. proton beam therapy [24]).

Limitations

All data were collected retrospectively from the medical records and thus the authors had little control over specificity or accuracy. In contrast to the reports of the neuropsychologic examination, the patients' medical records had very limited information on cognitive ability (i.e. the terms "mental retardation" or "compulsory special needs schooling" were referenced but not the specific IQ scores or the extent of the child's learning difficulties). We used references to special needs schooling as a proxy for cognitive impairment when only references to the former were present in the medical records.

Acknowledgements

We like to acknowledge the patients and their families, the generous support of the Swedish Childhood Cancer Foundation and the Jonas Foundation, and the staff of the Pediatric Neuro-Oncology Service at Skåne University Hospital (especially Charlotte Castor). Additional thanks are extended to Vibeke Horstmann for statistical guidance and Margareta Kihlgren, Ann Wirsén Meurling, Thomas Wiebe, Vineta Fellman, Karin Stjernqvist and Gunnel Ingesson for helpful advice and inspiration.

Ethics

This study was approved by the Swedish ethical vetting board of Lund.

Abbreviations

(C)RT: (Cranial) Radiation Therapy

ICP: Intra-Cranial Pressure

CNS: Central Nervous System

COG: Children's Oncology Group

VCTB: The Swedish Working Group for Pediatric CNS Tumors

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Tables
Manuscript: "Access to neuropsychologic services after pediatric brain tumor",
PNU-D-13-00264.

Table 1*:* Characteristics of and a comparison between the referred and not referred patients.

	Examined patients n=64	**Not examined patients,** n=68	**Total group** n=132	**P value**
Girls	34	24	58	0.053
Average age at first diagnosis	8.14	8.98	8.57	0.31
Astrocytoma	30	40	70	0.22
Treatment given				
Surgery	60	61	121	0.53
Chemotherapy	24	17	41	0.14
Locally admin. CRT	37	28	65	0.081
Whole brain RT	11	7	18	0.31
Average size of tumor at diagnosis (widest diameter)	3.85cm	3.10 cm	3.46 cm	0.015
Increased ICP at diagnosis	39	23	62	0.003
Deceased at the end of year 2006	5	9	14	0.40
One or more relapses	28	15	43	0.010
Neurocutaneous syndromes*	5	9	14	0.40
Ventriculo-peritoneal shunt or ventriculostomy	11	8	19	0.46
Epilepsy	7	8	15	1.00
Medication				
Hormone replacement therapy	22	20	42	0,58
Anti-epileptic drugs	8	11	19	0.62
Infratentorial/supratentorial tumor	33/31	28/40	61/71	0.30
Cognitive impairment, IQ<70	8	8	16	0.84
Cognitive impairment, IQ<80	8	7	15	

***** 11 pts with Neurofibromatosis I
2 pts with Neurofibromatosis II
1 pt with tuberous sclerosis