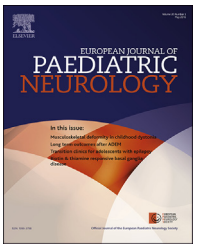
EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY XXX (2016) 1–8

Official Journal of the European Paediatric Neurology Society



Original article

Clinical characteristics and late effects in CNS tumours of childhood: Do not forget long term follow-up of the low grade tumours

Christoffer Ehrstedt [a,*,1], *Ingela Kristiansen* [a,1], *Gunnar Ahlsten* [a], *Olivera Casar-Borota* [b,c], *Margareta Dahl* [a], *Sylwia Libard* [b,c], *Bo Strömberg* [a]

[a] *Department of Women's and Children's Health, Uppsala University and Uppsala University Children's Hospital, Uppsala, Sweden*

[b] *Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden*

[c] *Department of Clinical Pathology and Cytology, Uppsala University Hospital, Uppsala, Sweden*

ARTICLE INFO

Article history:
Received 28 September 2015
Received in revised form
19 March 2016
Accepted 10 April 2016

Keywords:
Childhood
CNS-tumour
Cognitive
Late effects
Low grade

ABSTRACT

Aim: To investigate clinical characteristics and late effects of CNS tumours in childhood with a special focus on low-grade tumours, especially low-grade astrocytoma and glioneuronal tumours.

Methods: A retrospective population based study was performed at Uppsala University Children's Hospital, a tertiary referral centre for children with CNS tumours. Patients were identified from the National Brain Tumour Registry and the National Epilepsy Surgery Registry. Hospital medical records were analysed for patients with a follow up of ≥5 years after diagnosis. A re-evaluation of the neuro-pathological diagnosis was performed.

Results: A total of 193 patients (age 0–17.99 years) during a twelve-year period (1995–2006) were included; 149 survived ≥5 years. Three larger subgroups could be identified: astrocytic, embryonal and glioneuronal tumours. A supratentorial location was found in 52%. Medical late effects were mainly neurological and endocrinological, affecting 81% and 26% of surviving patients. Cognitive late effects were a frequent finding in the whole group but also in low-grade astrocytoma and glioneuronal tumours (53% and 67%). Thirty per cent had some kind of pedagogic support in school.

Abbreviations: CNS, Central nervous system; WHO, World Health Organization; NF-1, Neurofibromatosis type 1; NF-2, Neurofibromatosis type 2; TSC, Tuberous sclerosis complex; DNET, Dysembryoplastic neuroepithelial tumour; ICP, Intracranial pressure; OS, Overall survival; WISC, Wechsler Intelligence Scale for Children.

* *Corresponding author*. Department of Women's and Children's Health, Uppsala University, SE-751 85, Uppsala, Sweden. Tel.: +46 709409789, +46 186110114.

E-mail address: christoffer.ehrstedt@kbh.uu.se (C. Ehrstedt).

[1] Joint first authorship.

http://dx.doi.org/10.1016/j.ejpn.2016.04.009

Please cite this article in press as: Ehrstedt C, et al., Clinical characteristics and late effects in CNS tumours of childhood: Do not forget long term follow-up of the low grade tumours, European Journal of Paediatric Neurology (2016), http://dx.doi.org/10.1016/j.ejpn.2016.04.009

Conclusion: Late effects are common in long-term survivors of CNS tumours in childhood. Low-grade astrocytoma and glioneuronal tumours are no exception, and the findings support the need for long-term follow up.

1. Introduction

Central nervous system (CNS) tumours are, after leukaemia, the second most frequent malignant disease in children and constitute the most common form of solid tumours in childhood. The incidence of brain tumours in Sweden is 4.2/100,000 in children younger than 15 years of age[1] which is comparable to the other Nordic countries[2] and internationally reported figures.[3] In most reports the most common histologic tumour types are, in descending order, astrocytomas (38–45%), medulloblastomas/primitive neuro-ectodermal tumours (PNET; 12–25%), ependymomas (5–10%) glioneuronal tumours (5–8%) and craniopharyngiomas (4–6%).[1,3–7]

Survival rates, but also long-term neurologic and endocrine dysfunction as well as cognitive and psychosocial difficulties, vary greatly across different tumour types. Long-term complications in these domains are well recognised in the whole group,[8,9] especially among high-grade tumours (WHO grade III-IV)[10–15] but not to the same extent in low-grade tumours (WHO grade I-II).[16] Benign histology and favourable survival rates make it easy to miss possible long-term complications because the patients are considered cured and therefore lost to organised multidisciplinary follow up. Children with low-grade tumours are considered to be long-term survivors rather than having a life-threatening malignancy.[16] Although some studies indicate cognitive difficulties[11,13,16–19] there are few studies dealing with the long-term consequences of having had a low-grade brain tumour, with its impact on medical, cognitive, psychosocial functioning and quality of life.[20–25] This indicates a need for multidisciplinary studies in order to define an optimal medical follow-up and rehabilitation of children with both low- and high grade CNS tumours, and their families.

The aims of this retrospective study have been four-fold: 1) to describe the clinical characteristics, 2) to re-evaluate the neuropathological diagnosis in order to investigate the extent of diagnostic consensus, 3) to investigate the frequency of neurological, endocrinological and neuropsychological sequelae and 4) to investigate whether cognitive difficulties have been met by pedagogic interventions in school. These aims relate to the whole material and the most common tumour groups.

2. Material and methods

A retrospective population based study was performed at Uppsala University Children's Hospital, Sweden, a tertiary referral centre for children with CNS tumours. The referral centre serves six counties in Mid-Sweden with a population of 1.7 million people. Patient data were retrieved from the local and the National Brain Tumour Registry and the National Epilepsy Surgery Registry. All the 193 patients with a CNS tumour (age 0–17.99 years) diagnosed during a twelve-year period (1995–2006) were included. Hospital medical records were retrieved and scrutinized from paediatric, neuropaediatric, neurooncology, neurosurgery, neuropathology departments as well as neuropsychology records including pre- and postoperative neuropsychological assessments. Re-evaluation of the neuropathological diagnosis based on identification of histopathological criteria and immunohistochemical data, according to the current World Health Organization (WHO) Classification of Tumours of the Central Nervous System[7] was performed by two experienced neuropathologists in all eligible cases (i.e. biopsy undertaken). Original hematoxylin-eosin and immunohistochemically stained sections were re-evaluated. In some cases additional immunohistochemical analyses were performed in order to fulfil diagnostic requirements as defined in the WHO classification.

2.1. Ethics

The study was approved by the Regional Ethical Review Board (EPN Uppsala Log. No. 2010/229).

2.2. Statistics

The statistical analysis was performed with the SPSS statistical program, version 20. For comparing the different WISC domains obtained in the glioneuronal group to an IQ mean of 100 we used the one sample Wilcoxon signed rank test. The level of statistical significance was set at $p < 0.05$.

3. Results

The mean age at diagnosis was 9.0 years (median 9.8 years). The age distribution at diagnosis for the whole cohort is presented in Fig. 1.

There was a male dominance, with a male/female ratio of 1.4/1. There was no family history or increased risk of having a CNS tumour in the cohort, except in four cases with neurofibromatosis type 1 (NF-1) and two cases with von Hippel Lindau syndrome.

At presentation the majority (87%) had a medical history without any previous disease (data available for 188 patients). Ninety-seven per cent were regarded to evince normal psychomotor development. Five patients had delayed development: one had Down syndrome, one tuberous sclerosis complex (TSC), one Turner's syndrome and two delayed motor

Please cite this article in press as: Ehrstedt C, et al., Clinical characteristics and late effects in CNS tumours of childhood: Do not forget long term follow-up of the low grade tumours, European Journal of Paediatric Neurology (2016), http://dx.doi.org/10.1016/j.ejpn.2016.04.009