

POSTERIOR CRANIAL FOSSA LOW-GRADE GLIOMA IN CHILDREN: A CLINICOPATHOLOGICAL STUDY

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Objective - The aim of this study was to analyse the clinico-pathological characteristics, treatment, complications and outcome in patients with low grade astrocytomas (grade I and II).

Patients and Methods - This study was a retrospective analysis of 50 consecutive patients younger than 15 years who were hospitalized for surgical treatment of posterior cranial fossa tumours. The intracranial hypertension, neurological status, radiological CT or MRI findings, tumour localization, type of resection, hydrocephalus treatment, histopathology, complications and outcome were analyzed.

Results - There posterior cranial fossa tumours 25 (50%) children with astrocytoma among the posterior cranial fossa tumours. Of this number, there were 18 (72%) pilocytic astrocytomas and 7 (28%) ordinary histopathological subtypes of grade II astrocytomas. The average age in patients was 78.5 ± 40 months, patients with pilocytic astrocytoma 84 ± 43 months and patients with grade II astrocytomas 64 ± 27 months. The average size of pilocytic astrocytoma was 48 mm and the remaining grade II astrocytomas was 37 mm. The most common neurological deficit before and after surgery was ataxia. Paediatric patients with posterior cranial fossa low grade astrocytomas have evaluated postoperatively between 4 months to 98 months, in average 47.7 ± 25.9 and patients with grade II astrocytomas between 6 months to 103 months, in average 57.2 ± 38.4 .

Conclusion - Have a good prognosis after tumor total gross resection.

Key words: Pediatric brain tumours ■ Astrocytomas

Introduction

Tumours of the posterior cranial fossa occur more frequently in children than in adults. About 50-55% of brain tumours in children are infratentorial (1, 2). The most common location of these tumours is the cerebellar hemisphere (35-45%), then the vermis (15-20%), the fourth ventricle (15-20%) and the brain stem (13-18%). The most common histological types of these tumours are: astrocytomas, medulloblastomas and ependymomas. Astrocytomas are divided into four grades: grade I (fibrillary, protoplasmatic, gemistocytic), grade II which has three types (fibril, protoplasmatic and gemistocyte), grade III (anaplastic astrocytoma) and grade IV (glioblastoma multiforme). Pilocytic astrocytomas are the most frequent astrocytomas in children, accounting for 80% to 85% of cerebral astrocytomas. Juvenile pilocytic astrocytomas usually begin in the cerebellum, the brain stem, the hypothalamic region or the optical path, but they may also originate in other regions where astrocytes are present, including the cerebellar hemisphere and the spinal cord. The cerebellum is the most common site of origin of juvenile pilocytic astrocytomas (3). Other astrocytomas account for 15% to 20%. High grade astrocytomas in the posterior cranial fossa are rare.

The most common symptoms are associated with increased intracranial pressure as the result of the spatial compression caused by the tumour or hydrocephalus. Symptoms may include headache, nausea, vomiting, irritability, ataxia, visual disturbances and lesions of the peripheral nerves, depending on the location, size and speed of growth of the tumour (4-7).

The aim of the study was to analyse in patients with low grade astrocytomas (grades I and II) in the posterior cranial fossa the clinical, pathological characteristics, the frequency of symptoms or signs of intracranial hypertension, neurological findings,

radiological findings on initial and follow-up CT or NMR imaging, localization of the tumour, the scope of resection, the treatment of hydrocephalus, and the complications and outcome of treatment.

Patients and Methods

The study comprised a retrospective analysis of patients younger than 15 years hospitalized for surgical treatment of tumours in the posterior cranial fossa at the Neurosurgery Centre of Hopital Purpan in Toulouse (France) from 13 January 1992 to 28 December 2001. The study included patients who had complete medical documentation consisting of initial clinical findings, initial CT or NMR of the neurocranium, surgical results, and one or more post-operative follow up clinical, CT or NMR findings. In this period, 78 patients underwent surgery for posterior cranial fossa tumours of which 28 patients were excluded from the study (17 due to incomplete medical documentations, and 11 continued their treatment in other centres). The remaining 50 patients were the subjects of the analysis of this study. Histological classification was based on the criteria for classification of tumours recommended by the WHO (7, 8).

The presence of intracranial hypertension was diagnosed on the basis of clinical findings (headache, vomiting, papilla oedema), dilation of the ventricular system, and loss of subarachnoidal space on CT or NMR imaging of the neurocranium. The degree of ventricular dilation on CT or NMR is shown by the fronto-occipital horn ratio (FOR) (9). The age of the patients is shown in months. The size of the tumour is expressed in millimetres.

The scope of the resection of the tumour was analysed on the basis of follow-up CT with contrast performed 24 hours after surgery. Total resection is taken to be the

surgeon's belief that no tumour fragment remained in the operation field, and the absence of a zone of uptake of contrast on the post-operative CT. Subtotal resection is the presence of one minimal residual tumour fragment or the suspicion of minimal residue after post-operative CT using contrast medium. Partial resection is the presence of clear zones of uptake of contrast, whilst in some patients, only a biopsy was achieved. The outcome of treatment was monitored from the admission of the patient to the neurosurgical centre, to the last news on the patient.

Statistical analysis

Statistical analysis was undertaken using the MedCalc statistical software package (version 8.1.0.0 for Windows, MedCalc). The results are presented in absolute and relative numbers using mean values and standard deviations.

Results

There were 25 (50%) children with astrocytomas in the total number of posterior cranial fossa tumours analysed, of which 11 (44%) were girls and 14 (56%) boys. Of these patients with low grade astrocytomas, 18 (72%) had pilocytic astrocytomas, five (27.8%) girls and 13 (72.2%) boys, whilst 7

(28%) patients had grade II astrocytomas, six (85.7%) girls and one (14.3%) boy.

The average age of patients with low grade astrocytomas was 78.5 ± 40 months. Patients with pilocytic astrocytomas were aged from 24 months to 178 months, on average 84 ± 43 months, and patients with grade II astrocytomas were aged between 47 months and 160 months, on average 64 ± 27 months.

The most frequent locations of the pilocytic astrocytomas were the cerebellar hemisphere in 8 (44.4%), the brain stem in five (27.7%), the vermis in three (16.6%) and the fourth ventricle in two (11.1%) cases. Grade II astrocytomas were most often located in the brain stem, in five cases (71.4%), and in the cerebellar hemisphere in 2 cases (28.6%). The presence of cysts alongside the mural part of the tumour was verified in 12 (66.6%) patients with pilocytic astrocytomas and four (57.1%) patients with grade II astrocytomas.

The average duration of symptoms, before the diagnosis of the tumour was 4 ± 5.5 months in patients with pilocytic astrocytomas and 5.4 ± 8.4 months in patients with grade II astrocytomas. The frequency of symptoms and signs present in patients with pilocytic astrocytomas and grade II astrocytomas is shown in Table 1. Eleven patients (61%) with pilocytic astrocytomas and three patients with grade II astrocytomas had periventricular oedema.

Table 1 Symptoms and signs of 25 patients with pilocytic astrocytoma and astrocytoma grade II

Symptoms and signs	Type of tumor		Total
	Pilocytic astrocytoma n (%)	Astrocytoma grade II n (%)	n (%)
Headache	13 (72.2)	5 (71.4)	18 (72)
Vomiting	10 (55.5)	4 (57.1)	14 (56)
Ataxia	9 (50)	3 (42.8)	12 (48)
Static cerebellar signs	2 (11.1)	1 (14.2)	3 (12)
Cranial nerve dysfunction	2 (11.1)	1 (14.2)	3 (12)
Torticollis	3 (16.6)	1 (14.2)	4 (16)
Associated symptoms and signs	14 (77.7)	7 (100)	21 (84)

The size of the tumour at the time of diagnosis varied. There were four (22.2%) pilocytic astrocytomas below 30 mm, seven (38.8%) from 31mm to 50 mm, and there were also seven (38.8%) tumours measuring more than 51mm. There were four (57.1%) grade II astrocytomas below 30 mm, two (28.5%) between 31 mm and 50 mm and one (14.2%) above 51 mm. In total of the 25 tumours analysed, eight (32%) tumours were below 30 mm, nine (36%) were between 31 mm and 50 mm, and eight (32%) over 51 mm. Practically, 14 (77.7%) pilocytic astrocytomas were larger than 30 mm at the time of diagnosis and three grade II astrocytomas (42.8%).

The fourth ventricle could be identified on CT or NMR in all patients with grade II astrocytomas, whilst in 8 patients (44%) with pilocytic astrocytomas it was not possible to identify it. In most patients total or subtotal resection of the tumour was performed (Table 2).

The post-operative complications varied. In two patients with pilocytic astrocytomas pseudomeningocele occurred and cerebrospinal fluid (CSF) fistula in two. In two patients there were supratentorial hygromas and in one hydrocele testis. Also in one patient an abscess developed post-operatively in the surgical field, which caused hydrocephalus and was treated post-operatively by an external ventricular derivation (EVD). One patient had a local wound infection with osteitis. In the patients with grade II astrocytomas, in one case there was a supratentorial hygroma and one patient developed meningitis.

Both patients had a ventricular peritoneal derivation implanted post-operatively.

Hydrocephalus was treated by early ablation of the tumour with the use of corticosteroids, temporary implantation of an EVD before or during the operation, or implantation of a VPD (Table 3).

The neurological findings on the final evaluation of the patients varied. In the case of pilocytic astrocytomas, one patient had headaches, four were ataxic, one had static cerebellar signs and two persistent paresis of the cranial nerve. With grade II astrocytomas, in only one patient did the ataxia persist post-operatively. In total, with astrocytic tumours, at the time of release from hospital, one patient had headaches, five ataxia, in one patient there was persistent paresis of the nerve and in one static cerebellar signs. Patients with pilocytic astrocytomas were monitored for between four and 98 months post-operatively, on average 47.7 ± 25.9 and those with grade II astrocytomas for between 6 and 103 months, on average 57.2 ± 38.4 . Of 18 pilocytic astrocytomas operated on, 6 recurred, four of which after partial resection, one after total resection, one after sub-total and one after a biopsy. All partially resected tumours were located in the brain stem. In grade II astrocytomas there were no signs of growth of a tumour in this period of time, and in one patient on whom a biopsy was performed, radiotherapy and chemotherapy were given.

Table 2 Type of tumor resection

Type of tumor	Type of tumor resection				
	Total resection	Subtotal resection	Partial resection	Biopsia	Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Pilocytic astrocytoma	9 (36)	3 (12)	5 (20)	1 (4)	18 (72)
Astrocytoma grade II	3 (12)	-	2 (8)	2 (8)	7(28)
Total	12 (48)	3 (12)	7 (28)	3 (12)	25 (100)

Table 3 Treatment of hydrocephalus

Type of tumor	Treatment of hydrocephalus					Total n (%)
	VPD preoperative	EVD preoperative	EVD peroperative	EVD postoperative	Without derivation	
	n (%)	n (%)	n (%)	n (%)	n (%)	
Pilocytic astrocytoma	3 (12)	1 (4)	7 (28)	1 (4)	6 (24)	18 (72)
Astrocytoma grade II	3 (12)	-	1 (4)	2 (8)	1 (4)	7 (28)
Total	6 (24)	1 (4)	8 (32)	3 (12)	7 (28)	25 (100)

VPD = ventriculoperitoneal derivation

EVD = external ventricular derivation

Discussion

Brain tumours are one of the most serious illnesses of the central nervous system, especially if they are located in the posterior cranial fossa, where, in view of the limited space, rapid compression of the brain stem and herniation are possible (whether towards the foramen magnum or towards the tentorial incisura). Due to these dangers, urgent neurosurgical intervention is often required.

Of a total of 78 patients who underwent surgery for tumours in the posterior cranial fossa in the period from 13.01.1992 to 28.12.2001, the criteria for this study were met by 50 patients. In this period surgery was performed on 143 intracranial tumours in children, of which 78 (54.5%) were located in the posterior cranial fossa. This ratio is in line with studies already published (10, 11). Bruno et al. (11) presented a study of 1350 children with intracranial tumours in whom tumours in the posterior cranial fossa accounted for 54.7%.

Of these 50 patients, 29 (58%) were boys and 21 (42%) were girls. Of 25 astrocytomas analysed, 18 (72%) were pilocytic and 7 (28%) were grade II astrocytomas. As in other studies, pilocytic astrocytomas are the most common patho-histological form of astrocytic tumours (2, 4, 6, 12).

The age of the patients varied in relation to the patho-histological findings. With pilocytic astrocytomas they were aged from 24 months to 178 months and the average age was 84 ± 43 months, whilst with grade II astrocytomas they were between 47 and 160 months, with an average age of 64 ± 27 months, which is in line with most studies published so far (5, 13 - 17). Pilocytic astrocytomas were found in boys in 13 (72.2%) cases and in five girls (27.8%). Grade II astrocytomas, of which there were 7 in this study, were dominantly found in girls in a ratio of 6:1. The total relationship between the sexes for astrocytomas was 14 (56%) in boys and 11 (44%) in girls, which does not indicate any significant difference in terms of gender, as was also shown by earlier studies (5, 13, 15).

In both, pilocytic astrocytomas and grade II astrocytomas, signs of intracranial hypertension were dominant. The association of these symptoms was frequent in 14 (77%) with pilocytic and with grade II astrocytomas it was present in all 7 (100%) of cases. In total, associated signs occurred with astrocytomas in 21 cases (84%). This does not differ significantly from the data in the literature (13, 16 - 19).

In these studies, headaches occurred in between 76% and 85% of patients, vomiting in 65% to 74%, ataxia in 46% to 86% cases, and lesions of the cranial nerve in 29% to 37%. Disturbances of standing and gait were frequent, in 63% of 69% of cases, but these authors (13, 16 - 19) did not cite the frequency of this sign.

The duration of symptoms varied, depending on the patho-histological type. With pilocytic astrocytomas the average duration was 150 days and with grade II astrocytomas it was 120 days, which is in line with results published to date by certain authors (16, 19 - 21), for whom that period lasted for about 120 days. Ilgren and Stiller (18) published in their study that the average duration of symptoms was 18.7 months.

Practically, 14 (77.7%) pilocytic astrocytomas and 3 (42.8%) grade II astrocytomas were larger than 30 mm at the time of diagnosis. This fact shows that the clinical picture in pilocytic astrocytomas develops later than with grade II astrocytomas. However, 5 of 7 grade II astrocytomas were located in the brain stem, which may be the reason for the earlier manifestation of the clinical picture.

Tumours in the posterior cranial fossa may be of various consistencies. They may be solid, cystic, cystic with solid components, solid with intra-tumour micro-cysts and macro-cysts, and haemorrhagic or calcified zones. In our study we analysed the frequency of cystic components in individual types of tumours. In the case of pilocytic astrocytomas, cysts were present in 12 (66.6%) cases and in grade II astrocytomas in 4 cases (57.1%). Of 25 astrocytic tumours, cysts were present in 16 (64%).

Cystic formations in pilocytic astrocytomas are frequent and, according to certain authors, they occur in 70% to 85% of cases (22 - 24). In terms of the localization of the cystic formations, in pilocytic astrocytomas they were present in hemispheric locations in 7 (38.8%) patients, in the vermis region in 2

(11.1%) patients and in the brain stem region in 4 (22.2%). In 5 (27.7%) patients there were no cysts. Grade II astrocytomas were cystic in the hemispheres in 2 (28.5%) cases, and also in the brain stem in 2 (28.5%) cases. They were not cystic in the vermis, where there was only 1 (14.2%) tumour, and in two cases in the brain stem (28.5%). Of 25 astrocytomas 9 (36%) had cysts in the hemispheres, 2 (8%) in the vermis and 6 in the brain stem (24%). These figures are in line with certain studies already published. Ilgrin et al. (18) and Sgouros et al. (19) state that cystic astrocytomas are more frequent in the hemispheres. On the other hand, the frequency of cystic formations in the vermis was more frequent, in a ratio of 2:1, whilst in the studies mentioned this ratio was greater - to the advantage of solid tumours. Sgouros et al. (19) and Pancelet et al. (17) state that most astrocytic tumours in the brain stem are of a solid consistency, which was also confirmed by our analysis, where this ratio was 1.5:1.

Infratentorial tumours are a frequent cause of hydrocephalus, due to the obstruction of the CSF circulation in the posterior cranial fossa, where they cause internal hydrocephalus. Treatment of hydrocephalus caused by tumours in the posterior cranial fossa in children is still controversial. The classical options assume early extirpation of the tumour, with pre-operative use of corticosteroids (25) with or without an EVD (26) or on the other hand, the pre-operative implant of a VPD (27).

Those who favour the pre-operative implantation of a VPD justify this procedure for several reasons: a) gaining time for better preparation of the patient for the operation and undertaking additional neuro-radiological tests; b) it makes possible the better anaesthesiological preparation of the child for a complex surgical procedure; c) the surgical procedure is potentially safer when the intracranial pressure is normal. Albright et

al. (27, 28) point out that mortality in their series was lower with pre-operative implantation of a VPD. On the other hand many authors dispute this stance, pointing out its disadvantages: a) after extirpation of the tumour not all patients have the need for VPD; b) VPD may be a path for dissemination of the tumour (26), although others dispute this complication (29).

On the basis of the FOR index of 18 pilocytic astrocytomas, hydrocephalus was found in 13 (72.2%) cases, in grade II astrocytomas it was present in 6 (85.7%) cases. Of the 25 astrocytic tumours, hydrocephalus was present in 19 (76%) patients. In order to treat hydrocephalus, in our study, certain surgeons preferred ablation of the tumour, with or without implanting an EVD, with the previous use of corticosteroids, whilst others implanted a VPD pre-operatively. After treatment and evaluation of the patients, there was no hydrocephalus in our study.

Of 25 patients with astrocytic tumours, in 6 of them (24%) a VPD was implanted pre-operatively, in three patients (16.6%) with pilocytic astrocytomas and in 3 (42.8%) patients with grade II astrocytomas.

The number of children with a permanent VPD after surgery for a tumour in the posterior cranial fossa is between 10.5% and 36% (30, 31). There is a significant difference between the number of children who have a permanent VPD and the risk factor for the occurrence of hydrocephalus with infratentorial tumours (31), as well as a disagreement between certain authors about the systematic implantation of VPD and those who avoid this procedure.

The aetiological factors of juvenile pilocytic astrocytomas are unknown. Transformation into a malignant, high grade tumour is rare. Macroscopically, astrocytomas present as very well delineated tumour formations, which usually have a large cyst and a focal mural nodule. The tumour may also be solid, with or without cystic components.

Microscopically, juvenile pilocytic astrocytomas consist of well-differentiated pilocytes with hair-like glial extensions, associated with microcysts, which contain mucopolysaccharide material. Pilocytes are mixed with Rosenthal fibres, eosinophilic rod shaped bodies and granular eosinophilic bodies, which are usually found with indolent neoplasms. There is usually a capillary formation.

Juvenile pilocytic astrocytomas most often occur in the cerebellar hemisphere, are easily recognized on CT or NMR as well defined lesions with associated macrocysts. The nodular part of the lesion usually shows homogenous contrast staining. Calcification is present in 10% of juvenile pilocytic astrocytomas. Grade II astrocytomas show typical hypo-attenuation or hypo-intensity, they are unclearly defined lesions without post-contrast staining on CT or NMR.

Patients with juvenile pilocytic astrocytomas have better prognosis than patients with other forms of astrocytomas. During the post-operative follow-up of the patients, in our series, there were no fatal outcomes. The reason for this result is probably the short-term follow-up and the small number of patients. After total resection, if it is possible, the ten-year survival rate is 90%. After subtotal resection or biopsy, the ten-year survival rate is 45%. Morbidity depends on the localization of the tumour and the associated complications of the tumour resection.

The preferred radiological diagnostic technique with these tumours is NMR (32 - 35). The use of radiological findings alone to identify low grade gliomas results in incorrect diagnosis in about 50% of cases. NMR is useful in showing the stained tumour. Pilocytic astrocytomas are treated surgically. The tumour must be completely resected whenever possible. Post-contrast staining of the wall of the cyst may be seen on NMR, when this staining is present, it indicates the resection of the entire cyst (36 - 39).

Conclusion

The results of the study show that paediatric patients with pilocytic astrocytomas, as well as those with grade II astrocytomas, have a good prognosis after total resection of the tumour. In view of the limitations of the follow-up and the small number of patients in our series, it was not possible to estab-

lish the long-term prognosis. The treatment of hydrocephalus in paediatric patients with posterior cranial fossa low grade astrocytomas remains controversial.

Conflict of Interest: The authors declare that they have no conflict of interest. This study was not sponsored by any external organisation.

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