

THE CLINICAL CHARACTERISTICS OF MEDULLOBLASTOMAS IN CHILDREN

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Objective - This research was undertaken to analyse the clinical characteristics, treatment methods, complications and outcome in paediatric patients with medulloblastomas.

Patients and method - The study comprised a retrospective analysis of 13 consecutive patients younger than 15 years, who were hospitalized for surgical treatment of medulloblastomas. The clinical characteristics, radiology findings on the initial and control CT or NMR images, the localization and size of the tumour, the type of resection, the method of treatment of hydrocephalus, complications and outcome of treatment were analysed.

Results - There were 13 (26%) children with medulloblastomas in the total number analysed of tumours of the posterior fossa. The average age of the patients was 103±45 months. The average size of the medulloblastoma was 39 mm. The most common symptoms and signs were related to increased intracranial hypertension.

Conclusion - The best form of treatment of medulloblastomas is maximum surgical resection with the appropriate use of radiotherapy and/or chemotherapy depending on the age of the child.

Key words: Paediatric brain tumours ■ Medulloblastomas

Introduction

Tumours of the posterior fossa occur more often in children than in adults. About 50-55% of brain tumours in children are infratentorial (1, 2). The most common locations of these tumours are: the cerebellar hemisphere (35-45%), then the vermis (15-20%), the 4th ventricle

(15-20%) and the brain stem (13-18%). The most common histological types of these tumours are: astrocytoma, medulloblastoma and ependymoma. Medulloblastomas account for 30% of posterior fossa tumours in children, and 20% to 25% of all paediatric tumours (3-5). The mean age at the time of diagnosis is between 5 and 7 years, and more than 80% of cases are diagnosed before 16 years of age (6, 7). There are two time periods in which they occur most often, the first between 2 and 4 years and the second between 6 and 8 years of age (5,7). They are more common in boys than in girls, in a ratio of 2:1 (5-9). They most often develop in the part of the velum medulare inferior and, as they grow, fill the fourth ventricle of the brain and infiltrate the surrounding structures. These extremely malignant tumours, which belong to the primitive neuroectodermal group of tumours (PNET), infiltrate the floor of the fourth ventricle of the brain in about 30% of cases. They were first described in 1925 as spongioblastoma cerebelli (10). In 1930 Cushing published a major series on medulloblastomas. His publication encompassed 61 patients with cerebellar medulloblastomas, whose outcome was most often fatal (11).

The most common associated symptom is increased intracranial hypertension as the result of spatial compression by the tumour or hydrocephalus. Symptoms may include headaches, nausea, vomiting, irritability, ataxia, vision disturbances, and lesions of a peripheral nature depending on the location, size and pace of growth of the tumour (12).

The aim of this study was to analyse in patients with medulloblastomas the clinical characteristics, radiological findings on initial and control CT or NMR images, the location and size of tumours, treatment of hydrocephalus, the type of resection and complications, and the outcome of treatment.

Patients and methods

The study comprised a retrospective analysis of 13 patients younger than 15 years hospitalized for surgical treatment of medulloblastomas at the Neurosurgery Centre, Hôpital Purpan in Toulouse, France, from 13 January 1992 to 28 December 2001. Patients were included in the study who had complete medical documentation consisting of: initial clinical finding, initial CT or NMR of the neurocranium, surgical findings, and one or more post-operative control clinical and CT or NMR finding.

The presence of intracranial hypertension was diagnosed on the basis of clinical findings (headache, vomiting, papilla oedema), dilatation of the ventricular system and loss of subarachnoidal space on CT or NMR imaging of the neurocranium. The degree of ventricular dilatation on the CT or NMR is shown by the fronto-occipital horn ratio (FOR) (13). The age of the patient is shown in months. The size of the tumour is expressed in millimetres.

The extent of tumour resection was analysed on the basis of a control CT or NMR finding 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 or NMR. Subtotal resection is the presence of one minimal residual tumour fragment infiltrating the floor of the 4th ventricle less than 5 mm in size, or the suspicion of minimal residue after post-operative CT or NMR. 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

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

Results

Of the total number of paediatric patients analysed with tumours in the posterior fossa, 13 (26%) had medulloblastomas, of which 9 were boys and 4 girls. The age of the analysed patients was between 36 and 180 months, on average 103 ± 45 months. The patients were monitored post-operatively for between 2 months and 96 months, on average 39 ± 35.3 months.

The duration of symptoms before diagnosis of the tumour was from one day to 180 days, with an average of 59.5 days. In 3 patients the clinical picture was dominated by signs of intracranial haemorrhage, whilst in the other 10 patients the signs of intracranial hypertension manifested themselves gradually. Headaches were present in 12 patients, accompanied by vomiting in 10 cases. Static cerebellar syndrome was present in 8 patients, whilst paralysis of the cranial nerve occurred in 4 cases and torticollis in one patient. Acute abdominal pain was present in one girl, after which signs of intracranial haemorrhage appeared. A drop in success at school and lack of interest in daily activities occurred in one boy. The association of these symptoms and signs was present in 10 cases.

The most frequent location of the medulloblastomas was in the vermis in 12 cases, of which infiltrated the floor of the 4th ventricle. In one case the medulloblastoma filled the cerebellopontine angle the origine of the tumor was in the hemisphere of the cerebellum. Of the 13 cases, in 2 the tumours were smaller than 30 mm, and in the other 11 they were between 31 mm and 50 mm in size. Cystic components were present in 3 cases, and haemorrhagic components in 3 cases. At the point of diagnosis, metastasis was present in 2 patients with medulloblastomas.

The 4th ventricle could be identified on the initial CT or NMR in 8 cases. On the basis of the pre-operative FOIP, the presence of hydrocephalus was diagnosed in 10 patients, whilst hydrocephalus occurred post-operatively in one patient. Hydrocephalus was treated by early tumour ablation with the use of corticosteroids, temporary implantation of an external ventricular derivation (EVD) before or during the surgical procedure, ventriculoparitoneal derivation or implantation of a ventriculoparitoneal derivation (VPD). The method of surgical treatment of hydrocephalus is shown in Table 1.

In one patient the EVD was implanted postoperatively due to meningitis accompanied by hydrocephalus, and he subsequently had a VPD implanted.

In most cases total or subtotal resection was performed. The type of resection is shown in Table 2.

Adjuvant therapy was prescribed in 12 patients (since 1 died postoperatively). For 11 patients radiotherapy and chemotherapy was prescribed, whilst in one only chemotherapy was prescribed (aged under 3 years).

Table 1 Preoperative treatment of hydrocephalus

Treatment of hydrocephalus	No. of patients
Ventriculocisternostomy	1
Ventriculoparitoneal derivation	3
Preoperative external ventricular derivation	4
No derivation	2

Table 2 Type of tumour resection

Resection	No. of patients
Total	5
Subtotal	3
Partial	5

Table 3 Postoperative complications related to the cerebrospinal fluid system

Postoperative complications	No. of patients
Pseudomeningocele	2
Leakage of cerebrospinal fluid	2
Supra or infratentorial hygromas	2
Ventriculoparitoneal derivation dysfunction	1

Postoperative complications were most often related to the cerebrospinal fluid system and are shown in Table 3.

In three patients meningitis occurred postoperatively, and epilepsy in one, whilst one patient died.

At the time of the last evaluation, metastasis had appeared in two patients after partial resection (in one after two months, and in the other after 4 months). Both patients died within the following 20 days. After total and subtotal resection, metastasis appeared in the spinal canal in one patient after 12 months. In one there was a relapse after 48 months. The most common persistent neurological deficit was static cerebellar syndrome. Also, in patients treated by radiotherapy, there was a drop in mental function and hormonal disturbances. Paresis of the sixth cranial nerve and nystagmus were present in one patient.

Discussion

The average age of the patients with medulloblastomas analysed in our study was 103 ± 45 months, which is slightly above the average age published in earlier studies, where it was between 60 months and 84 months. However, the age of our patients is in accor-

dance with the fact that more than 80% of medulloblastomas appear before the age of 16 years (6, 7). The ratio of boys to girls of 2.2:1 is in line with the data in most published studies (5, 9, 14).

The duration of symptoms before diagnosis of the tumour was from 1 day to 180 days, on average 59.5 days, which is in correlation with earlier studies, where this period was between a few days and 6 months, on average 6 to 7 weeks.

The clinical picture was dominated by signs of increased intracranial hypertension. These signs developed gradually in most patients. The signs of increased intracranial hypertension with medulloblastomas occur much earlier and develop more quickly than in astrocytic tumours (3, 15), which was also seen in our study. The signs of increased intracranial hypertension, headaches and vomiting, may be wrongly interpreted at first, since they are often accompanied by abdominal pains, so these children are sometimes subjected to gastroenterological tests over several weeks, or an appendectomy is even performed as was the case with one of our girls. Mood disorders are frequent and characterised by apathy, indifference or even aggression, a drop in success at school or sleep disturbances, most often accompanied

by sleep inversion. This clinical picture was present in one boy in our study.

The clinical picture of medulloblastomas may also develop rapidly, most often due to intratumoral haemorrhage, and then most often accompanied by signs of subarachnoidal haemorrhage or acute intracranial hypertension, which was also seen in our study, where the clinical picture developed in this way in almost 1/4 of the patients. Also, intratumoral haemorrhage may be wrongly interpreted in terms of aetiology, which was the case in one girl in our study, where previous bleeding (two months before the diagnosis of medulloblastoma) was interpreted as haemangioma cavernosum.

Tumours in the posterior fossa may have various consistencies. They may be solid, cystic, cystic with solid components, solid with intra-tumour microcysts or macrocysts, haemorrhagic or calcified zones. Medulloblastomas had cystic components in 3 (23%) cases, whilst some authors cite frequency of cysts as in between 40% to 75% of cases (16-18). Intratumoral haemorrhage was present with medulloblastomas in 3 (23%) patients, whilst in Laurent's study (19) it was present in 11%.

At the moment of radiological diagnosis, the medulloblastomas had produced metastatic deposits in 2 (15.3%) cases, which is in line with the results published previously from earlier studies, where that percentage of dissemination was between 11% and 71% (20, 21). It is especially important to establish the existence or absence of metastasis at the time of radiological diagnosis, since this is an important prognostic factor. For this reason it is vital to perform an NMR of the spinal canal before surgery, as well as NMR of the neurocranium, since a postoperative NMR, due to the presence of blood and haemostatic substances (Surgicel, Spongostan), may give a false positive result. On the other hand, if metastatic disease is present, surgical

intervention is not required except for palliative reasons, in view of the significant postoperative morbidity and the lack of possibility of radical resection.

Treatment of hydrocephalus in posterior fossa tumours is still controversial. In order to treat hydrocephalus with medulloblastomas, some surgeons prefer ablation of the tumour with or without inserting an EVD, with the previous use of corticosteroids, whilst others prefer preoperative implantation of a VPD. Also, some authors prefer ventriculocysternostomy. Practically, 4 (30.7%) patients had a permanent VPD, which is in line with results from earlier studies, where the percentage was between 10% and 40% (22-24). Ventriculocysternostomy, as a method to create internal derivation of the cerebrospinal fluid, could reduce the number of VPDs significantly.

Medulloblastomas are soft, infiltrative tumours, which in 30% of cases infiltrate the floor of the 4th ventricle, so their resection is often limited. The part that infiltrates the floor of the 4th ventricle does not need to be extirpated. Since they are radiosensitive tumours, subtotal resection is acceptable.

Early postoperative complications are mostly linked to the cerebrospinal fluid system, which is to be expected in view of the fact that the tumour is located within the fluid canals and its extirpation requires opening them. At the time of the last evaluation, the most common neurological deficit was static cerebellar syndrome, which was the result of the preoperative location of the tumour and surgical manipulation while it was being extirpated. Patients who were treated by radiotherapy, alongside static cerebellar syndrome, also had a significant fall in mental function and hormonal deficit.

Metastatic deposits appeared in the patients in our study much earlier after partial resection than after total or subtotal resection, which indicates the importance of perfor-

ming the maximum possible resection of the tumour. Relapse of medulloblastoma most often occurs within 2 to 4 years after surgery (14, 25), which is also visible from our study. In view of the short time of postoperative follow up of our patients, it was not possible to examine long-term survival and later relapses.

The use of chemotherapy for medulloblastomas together with radiotherapy resulted in significant benefits, especially in terms of tumour residue, tumours affecting the brain stem and metastatic lesions (8, 26). Currently, after surgery and combined use of radiotherapy and chemotherapy in children with non-disseminated medulloblastomas, the possibility of five-year survival is 80% or more, from the time of diagnosis and treatment (27). Children younger than 3 years have significantly poorer prognosis and for them the five year survival rate is from 20% to 40% (28, 29), because these patients cannot be treated with radiotherapy (30), or, on the other hand, because dissemination of

the illness at the time of diagnosis is more common in younger children (31).

Conclusion

Treatment of medulloblastomas is still accompanied by significant mortality and morbidity. Most commonly metastasis appears after 12 months following treatment, and after partial resection. The best form of treatment is the maximum possible resection with the use of adjuvant therapy. The choice of treatment of hydrocephalus with medulloblastomas, as in other tumours of the posterior fossa, remains controversial.

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