A Giant Hyperostotic Parasagittal Meningioma in a Child with Neurofibromatosis Type II. A Case Report and Literature Review


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Large parasagittal meningiomas, in particular hyperostotic ones, in children are rare and problematic in the differential diagnosis. The literature reports only single clinical cases related to this issue; opinions about the indications, surgical treatment options, and prognosis are contradictory. This paper presents a clinical case of a hyperostotic parasagittal meningioma with intra- and extracranial growth in a 10-year-old boy with neurofibromatosis type II, which significantly worsened the prognosis. We discuss the epidemiological and clinical features of childhood meningiomas and issues of their diagnosis, treatment, and prognosis.

Keywords: parasagittal, meningioma, hyperostosis, children, neurofibromatosis.

Meningiomas diagnosed in children under the age of 15 years form a special group and have a number of principal differences from meningiomas in adults. Parasagittal meningiomas are less common in children than in adults and account for only 4% of all brain tumors [1]. Hyperostosis can occur in association with convexity and parasagittal meningiomas [2]. In childhood, 25—49% of meningiomas are associated with hyperostosis [3—6], while in adults, this figure amounts to 4.5% [2]. In children, 33—40% of meningiomas are associated with neurofibromatosis type II (NF-2) [3, 6—8], which is a factor worsening the disease prognosis [1, 3, 9].

In this article, we present a rare clinical case of hyperostosis associated with a giant parasagittal meningioma with intra- and extracranial growth in a child with NF-2.

Clinical case

A 10-year-old boy L. applied to the Neurosurgical Institute (August 31, 2015) with complaints of a bulging in the parietal region. Eleven days before hospitalization, the patient had acutely developed right-sided hemiparesis and hemihypesthesia that completely regressed within 8 days of conservative treatment, including osmodiuretics and glucocorticoids. Careful taking of a family history revealed that the child’s grandmother had bilateral neurinomas of the vestibulocochlear nerve (absolute diagnostic criterion for NF-2 [10]), and his mother died of an unspecified brain tumor (she refused surgery, so there was no histological verification). MRI of the brain detected a large parasagittal tumor with intra- and extracranial growth, perifocal edema, and involvement of the parietal bones, which invaded the middle third of the superior sagittal sinus (Fig. 1).

At admission, there were no focal neurological and intracranial hypertension symptoms. The Karnofsky scale score was 100. On examination, a tight elastic bulging in the temporal parasagittal region, mostly on the left, was found. The time of its emergence was unknown. No subcutaneous neurofibromas were found. SCT of the brain revealed a parasagittal contrast enhanced tumor as well as a hyperostotic lesion of both parietal bones, 11×8.5 cm in size, with a marked periosteal reaction (Fig. 2). According to total selective cerebral angiography, the afferents feeding the tumor were multiple small branches of the ICA and ECA; the superior sagittal sinus was not enhanced at the tumor site (Fig. 3).

Given the history, examination, and radiographic findings, including intra- and extracranial components of the tumor and the bone lesion, the diagnosis was...
To determine the tactics of treatment, an open biopsy of the extracranial portion of the tumor was performed (03.09.15). The biopsy revealed meningotheliomatous meningioma, WHO Grade I, with a Ki-67 labeling index of 5—7%. An attempt to resect the tumor was made (10.09.15). Resection of the extracranial tumor component and resection trepanation of the skull with removal of hyperostosis were performed through a horseshoe-shaped skin incision in the projection of the affected calvarial area. This procedure exposed the intracranial tumor portion, but surgery was terminated due to a high blood loss and a high risk of further massive bleeding. At the second stage, 8 days later, the intracranial tumor portion was removed. The superior sagittal sinus walls occurred to be the initial site of tumor growth. Because of marked venous bleeding from the sagittal sinus, a drop in arterial pressure, and the risk of impairment of venous outflow from large vessels of the parietal region, total removal with resection of the ICA was not performed. The ICA wall was strengthened with tachocomb and artificial DM. The extent of tumor resection was Simpson grade 4 [11]. According to the pathology report, the resected intracranial meningioma portion was identified as atypical meningioma, WHO Grade II. On September 23, 2015, the patient underwent duraplasty (artificial sheath) and bone defect reconstruction using Palakos (Fig. 4). The patient was discharged home 2 weeks after surgery. By that time, the child was active, walked around the department, played, communicated with others, and was capable of self care. The Karnofsky scale score was 100.

One month later, control MRI of the brain revealed small residuals of the meningioma in the superior sagittal sinus region (Fig. 5). Given the family history, MRI of all parts of the spinal cord was also performed, which revealed a space-occupying lesion at the C6—C7 space level on the left, most likely neurinoma, which did not clinically manifest itself (Fig. 5, 6). Thus, the child had a combination of the intracranial meningioma, neurinoma of the C6—C7 spinal nerve, and family history (a direct relative with NF-2), which was the basis to diagnose neurofibromatosis type II.

Three months after tumor resection, the patient underwent a course of stereotactic radiation therapy at a dose of 60 Gy in 30 fractions for the residual meningioma. Control MRI of the brain at 6 and 12 months after surgery did not detect continued growth. Further radiation treatment for the neurinoma at the C6—C7 level was under discussion.

Discussion

The annual incidence rate of meningiomas increases with age and peaks at 8.4 per 100,000 population by the eighth decade of life [12]. Meningiomas account for 13—25% of all adult intracranial tumors [13]. At the same time, the occurrence of these tumors in children is much lower and is only 0.4—4.6% [1, 3, 14]. Adult meningiomas are more common in females [9, 12]; on the contrary, pediatric meningiomas are more common in boys [1]. However, according to some studies [4], the primary incidence of meningiomas is approximately the same in children of both genders. Pediatric meningiomas are associated with hyperostosis in 25—49% of cases [3—6], while this parameter is 4.5% for adult tumors [2].

The topography of pediatric and adult meningiomas is also different. Convexity meningiomas account for 41% of pediatric meningiomas [1] and only 19% of adult,
meningiomas [15]. Parasagittal pediatric meningiomas are rare (about 4% of cases [1]) in contrast to adult tumors (25% of cases [15]). In addition, pediatric meningiomas are often (about 15% of cases) found in the ventricle cavity [1, 4].

Y. Liu et al. [1] (2008) analyzed a large number of pediatric meningiomas and concluded that the prognosis was primarily affected by the following factors: the extent of initial resection (total resection is associated with a better prognosis), location of the tumor (affects the completeness of resection and, indirectly, the prognosis), presence of NF-2, and previous radiation treatment for other tumors (worsens the prognosis). In 33—40% of cases, pediatric meningiomas are associated with neurofibromatosis type II [3, 6—8]. Neurofibromatosis type II is believed to increase the risk of recurrence and death in meningiomas [1, 3, 9, 16]. At the same time, the degree of anaplasia is a less significant factor [1].

Bilateral neurinomas of the VIIIth nerve are the absolute diagnostic criteria for NF-2 [10, 17]. Also, the diagnosis of NF-2 is established if there is a direct relative having this disease in a combination with either unilateral neurinoma of the VIIIth nerve or two or more of the following signs: neurofibroma, meningioma (one or more), glioma (one or more), schwannomas (including one or more spinal schwannomas), and juvenile posterior subcapsular lenticular cataract [10, 17]. Cafe-au-lait spots occur in approximately 80% of NF-2 patients but have no diagnostic significance [10].

The main method to diagnose meningiomas is MRI. Meningiomas sometimes invade vital vascular structures, so direct selective cerebral angiography is an important
adjunctive diagnostic technique in the preoperative period. In addition, in the presence of large feeding vessels, the vessels can be embolized to reduce blood loss at the main stage of treatment [3, 18].

As early as 1987, K. Kim et al. [19] emphasized the importance of spiral computed tomography for the diagnosis of tumors associated with hyperostosis. The authors noted that hyperostosis associated with convexity or sphenoid wing meningiomas may often be confused with bone changes associated with other pathological processes, such as fibrous dysplasia, osteoma, or sarcoma. All 9 cases presented in the study had one or more CT features typical of hyperostosing meningiomas, namely: a pronounced periosteal reaction, inward bulging of the bone in the lesion area, an irregular eroded surface of the affected bone, and intracranial changes. The authors [19] argue that high-resolution computed tomography is the method of choice for evaluation of hyperostosis and differential diagnosis of hyperostosing meningiomas and other diseases. The literature [18, 20, 21] reports only single cases of meningiomas associated with hyperostosis in children. The presented clinical case is rare and of great interest because of the medical history features and the complexity of differential diagnosis. Before the tumor biopsy, one of the presumptive diagnoses was a meningioma in the setting of neurofibromatosis type II. However, the patient did not fully meet the diagnostic criteria: having a direct relative with bilateral neurinomas of the VIIIth nerve, the patient himself had a single tumor and no neurinomas by the time of hospitalization. A giant meningioma in the child without neurofibromatosis was unlikely. MRI and CT findings might equally indicate hyperostosing meningioma and Ewing’s sarcoma. Therefore, the second potential diagnosis was primary Ewing’s sarcoma of the cranial vault. This diagnosis was favored by a short history of just 11 days after the onset of symptoms and location of the tumor — the parietal and frontal regions that are typical primary sites of Ewing’s sarcoma growth [22]. In addition, bone changes associated with this tumor can be characterized either by lysis of the inner and outer bone plates or by sclerosis of bone tissue with a periosteal reaction in the form of spicules, which is hardly distinguishable from hyperostosis in meningioma on CT images.

In the world practice, both tumor resection and neoadjuvant chemotherapy are used as the primary treatment for Ewing’s sarcoma [22—25]. Chemotherapy can be selected as primary treatment in the absence of symptoms of intracranial hypertension [25]; in our case, there was no intracranial hypertension. If treatment starts with chemotherapy, the 5-, 10-, 15-, and 20-year overall
The survival of patients with Ewing’s sarcoma is 57.2, 49.3, 44.9, and 38.4%, respectively [26].

The standard of treatment for meningiomas is surgical resection. However, total resection is achieved only in 80—90% of patients [3]. The surgeon should strive for total resection of convexity and olfactory meningiomas as well as meningiomas of the anterior third of the cerebral falx and the superior sagittal sinus.

Fig. 6. MRI scans of all parts of the spinal cord of the 10-year-old patient L. A neurinoma at the C6―C7 level on the left is indicated by arrows.
At the same time, if the tumor is located in the medial sphenoid wings, posterior superior sagittal sinus, clivus, or orbit, subtotal resection is safer treatment [18, 27]. Based on these factors and the diagnosis, a treatment approach is chosen. After an open biopsy and receiving the results of a histological study, the diagnosis and the need in maximally radical surgery became apparent.

According to the literature [28], adjuvant radiation therapy significantly improves local tumor control in atypical and malignant meningiomas, especially in cases of subtotal resection. Despite the fact that the difference in disease-free survival after surgical and combined treatment of meningiomas was not statistically significant in most studies [28], some authors have still found a significant difference confirming the positive effect of radiotherapy on disease-free survival [29]. For example, I. Piscevic et al. [29] (2015) reported the following results: out of 88 meningioma patients, 58 patients had recurrence within a mean follow-up period of 5.6 years. Five-year disease-free survival (DFS) in patients who underwent tumor resection followed by radiotherapy at a dose of 55/60 Gy (n=34) was 65%, and that in patients who underwent surgery alone (n=24) was 13%. The differences were statistically significant (Log rank=31.9; p=0.001). For atypical meningiomas, the DFS difference was even more significant (Log rank=34.1; p=0.001): the 5-year DFS in combined and surgical treatment groups was 75 and 12%, respectively. It should be noted that the literature lacks studies devoted to the efficacy and safety of radiation therapy in pediatric meningiomas, and patients with neurofibromatosis have been excluded from most similar studies.

Unlike patients with sporadic tumors, patients with NF-2 often have multiple or extensive tumors and a high risk of recurrence [1, 3, 9, 16], which in some cases limits the capabilities of surgery and radiotherapy. Pharmacological therapy with proven efficacy in meningioma patients is currently not available. However, a better understanding of the molecular mechanisms of NF-2 pathogenesis opens the opportunity for application of targeted therapy.

Tumor growth is often accompanied by neovascularization, therefore tumors produce angiogenic factors, such as the vascular endothelial growth factor (VEGF) [30]. A VEGF inhibitor is the medication bevacizumab [30]. This is a humanized monoclonal antibody that prevents binding of all VEGF isoforms to VEGF receptors. A study by F. Nunes et al. [31] (2013), which evaluated a meningioma response to bevacizumab treatment in NF-2 patients, demonstrated that a partial response (a decrease in the tumor size by more than 20%) was received in 30% of the patients. A gradual decrease in the tumor in patients on treatment lasted for 3.7 months, on average, and then the size remained stable. The mean duration of remission was 15 months.

Despite the fact that bevacizumab is effective only in a third of patients, targeted therapy may be used in meningioma patients in the setting of NF-2 if other anti-recurrence treatments fail.

Conclusion

In the presented case, the cause to use staged surgery was poorly controlled bleeding at all stages of soft tissue manipulations and tumor resection, which may lead to a significant blood loss and serious complications. The staged surgical treatment enabled resection of the extra- and intracranial tumor portions, followed by reconstructive closure of the bone defect without negative somatic and neurological effects, as well as good and rapid functional recovery of the patient.

In conclusion, it is necessary to emphasize the importance of a careful taking of family and hereditary history as well as MRI of not only the head but all parts of the spinal cord in children operated on for meningiomas. In the presented case, this facilitated identification of an asymptomatic neurinoma at the cervical level, establishment of the diagnosis of NF-2 (negatively affecting the prognosis), and adjustment of the treatment.

There is no conflict of interest.

**REFERENCES**


The paper describes and discusses a rare clinical case that is also of great theoretical importance. The work is easy to read and well illustrated. The discussion of the case and comparison with the literature data provide the reader with an adequate view of the issue and the current state of the problem. The article is of great interest to a wide range of neurooncologists and neuropediatricians.

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Commentary

The presented observation is a rare case of neurofibromatosis type II combined with parasagittal meningioma in a child and is devoted to solving topical issues of neurosurgery, in particular, modern treatment options for primary brain tumors. This problem is important for several reasons related to improvement of diagnostic methods, new capabilities of the modern microneurosurgical complex, and an increase in the resectability of this complex group of patients. Undoubtedly, surgery is believed to be the main modern technique in complex treatment is surgical, but the tactics of surgical treatment, choice of an operative approach and methods that increase the radicalness of tumor resection still remain controversial, which causes increased interest in this clinical case and confirms the topicality of the problem.

The tumor nature of hyperostosis in meningiomas is now generally recognized. However, invasion of the dura mater and bone by the tumor and formation of hyperostosis are not considered as signs of biological aggressiveness, and hyperostosis associated with parasagittal meningiomas has no effect on recurrence. Only an increased number of recurrences in the case of bone destruction or hyperostosis combined with destruction have been observed. Head soft tissue invasion by meningioma is considered as an indicator of biological aggressiveness of the tumor.

The literature emphasizes a high recurrence rate of parasagittal meningiomas, which is associated with anatomic limitations of surgical radicalness in this area. Parasagittal meningiomas affect the superior sagittal sinus in 15—50% of cases, which sometimes objectively complicates one-stage resection of the tumor. In these cases, surgery should be broken up into several stages. Anatomical data should be considered when planning and evaluating outcomes of surgical treatment.

The presented work provides a detailed, critical, and chronological analysis of the literature data on neurofibromatosis type II associated with meningiomas. The authors rightly put emphasis on insufficiently resolved issues of this complex pathology.

This clinical case is of considerable scientific and practical interest and is devoted to the solution of topical issues of neurosurgery and neurooncology. The work is well illustrated and written in a good literary language and may serve as a guide for both novice neurosurgeons and experienced specialists.

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