Intermediate-Grade Meningeal Melanocytoma in a 19-Month-Old Child with Difficulties in Differential Diagnosis and Management

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ABSTRACT

Intermediate-grade meningeal melanocytoma (IGM) is a rare tumor that has not been reported in children so far. It is speculated to have more aggressive clinical behavior with undefined best management options. In this study, we present a 19-month-old girl as the first case with IGM in English literature. Preoperative diagnosis was ambiguous, given the unclear patient history and radiological features resembling a growing skull fracture or a congenital parietal bone agenesis subtype. During surgery, a dark gray-black dural area (5 × 7 cm in size) was found and then excised. However, the surgery was complicated due to brain edema and swelling, warranting a second surgery for reconstruction and dural repair. Of the 16 reported adult patients, 14 showed a high recurrence rate without adjuvant radiotherapy; 2 showed no recurrence with adjuvant radiotherapy. No adjuvant radiotherapy was given to our patient since she was 19 months old at the time of diagnosis and showed no recurrence at 48-month follow-up until now. Close monitoring with radiological imaging is of paramount importance for such cases.

KEYWORDS: Melanocytic tumor, Growing skull fracture, Children, Intermediate-grade

INTRODUCTION

Meningeal melanocytomas are a rare group of benign tumors in the central nervous system, classified as grade I according to the WHO (World Health Organization) 2016 classification of tumors of the central nervous system (3,15). However, an extremely rare subset of these lesions has a certain type of aggressive histopathological feature classified as intermediate-grade meningeal melanocytoma (IGM) (3). They have been speculated to have more aggressive clinical behavior. It is unknown whether IGM management may need a different approach than that of benign meningeal melanocytomas since there are only 16 cases reported to date (5,26,27). A precise algorithm needs to be established. Here, we report the first pediatric IGM in a 19-month-old girl, which was initially misdiagnosed as a growing skull fracture or a congenital parietal bony defect.

CASE REPORT

A 19-month-old girl was admitted to the neurosurgery department with an abnormal head shape, softness, and bony deficit on the left side, which became apparent over time. There was no clear history of trauma. She was on follow-up by a physical therapist due to a slight gait disturbance. In neurological and physical examinations, the patient showed no abnormality other than the slight gait disturbance and bilateral inverted foot. On brain computed tomography (CT) scan, large bony destruction in the left posterior frontoparietal areas with cerebral herniation from deficit area was found (Figure 1). The mass-like enlargements were thought to be nonspecific and regarded as blood products since magnetic resonance imaging (MRI) did not correlate with mass lesion (Figure 1). With these findings, growing skull fracture was suspected despite a clear history of no head trauma. Congenital parietal
bone agenesis was also suspected due to gait disturbance presence and bilateral inverted foot in the history. During surgery, after skin incision, a 5 × 7 cm dark gray-black dural area was observed with occasional thickening in some regions, which was excised thoroughly. However, duraplasty and bony reconstruction were impossible due to brain edema and swelling. After an appropriate anti-edema therapy for 10 days, cerebrospinal fluid leakage mandated a second surgery for dural repair, and thorough bony reconstruction using artificial grafts was performed. Microscopic examination showed nodular, trabecular, and diffuse areas of the tumor composed of polygonal-shaped epithelioid cells with large eosinophilic cytoplasm, vesicular nuclei, and prominent nucleoli (Figure 2A). In some areas, tumor cells were forming pseudocystic spaces. There was heavy melanin pigment in the tumoral cells’ cytoplasm, especially in areas showing pseudocystic arrangement (Figure 2B). Melanin-containing macrophage accumulation was also seen in intervening stroma between tumor cells. There was slight pleomorphism and rare mitotic figures (1–2/10 hpf), but no necrosis. Additionally, there was a bone invasion. Neoplastic cells were diffuse positive for HMB-45 and S100 and negative for desmin, GFAP and epithelial membrane antigen. MIB-1/Ki-67 proliferation index was 10% (Figure 2C–D); K-RAS and N-RAS mutations were negative, and no BRAF V600E mutation was detected by polymerase chain reaction. The case was diagnosed as IGM. The patient did well after discharge, with no oncologic therapy provided, and showed no relapse, recurrence, or neurological problem during the 4-year follow-up (Figure 1).

DISCUSSION

The central nervous system’s primary melanocytic tumors are classified as meningeal melanocytosis, meningeal melanocytoma, meningeal melanoma, and meningeal melanomatosis by the WHO 2016 classification (15). Meningeal melanocytosis and meningeal melanocytoma are benign lesions, which are classified as grades 0 and I, respectively, while meningeal melanoma and meningeal melanomatosis are malignant lesions, which are classified as grade III. These lesions primarily develop in the central nervous system and

Figure 1: Preoperative and postoperative radiological images: A, B, and C) The patient’s preoperative magnetic resonance imaging (MRI) and computed tomography (CT) scans showing brain herniated from a bony deficit at the left posterior frontoparietal areas. In the absence of contrast-enhanced MRI, no mass lesion was noticed, leading to growing skull fracture or congenital parietal bone agenesis suspicion. D) Early postoperative CT after reconstruction. E) MRI at 1-month follow-up. F) Contrast-enhanced T1-axial MRI at 24-month follow-up with no recurrence.
are thought to be of similar origin representing the benign and malignant ends of the spectrum (14). Although it is suggested that all melanomas of the central nervous system may be metastatic; metastatic melanomas have different clinical and histological features, and recent studies do not support this theory (10).

Meningeal melanocytomas are benign extra-axial tumors arising from leptomeningeal melanocytes of embryonic life’s neuroectoderm. Proportional to melanocyte distribution, these lesions are usually located at the upper spinal cord and posterior fossa (23), and are rare in the central nervous system and common in adults with reported female preponderance (12). They are usually solitary; however, multifocal lesions and suspected spinal seeding are still reported (1,2). Additionally, malignant transformation of these lesions is reported (21,24,28,29).

A small subset of primary melanocytic lesions was first defined as IGM with histological and clinical features by Brat et al. (3). These lesions were described to have relative hypercellularity but lack high mitotic rate, cytological atypia, and anaplasia seen with melanomas; however, microscopic invasion to the central nervous system may be observed. MIB-1/Ki-67 labeling index is also used as a parameter for classifying melanocytic lesions. Melanocytomas have been reported to have MIB-1/Ki-67 values up to 4–5%, while melanomas typically have values >8–10% (4,9,21). Although MIB-1/Ki-67 values falling between these figures can be an indication for IGMs, there is no established threshold value. In previous studies, there are reports of lower or higher values of IGMs and melanocytomas and melanomas having >5% and 2%, respectively (24,26).

In our patient, MIB-1/Ki-67 labeling index was 10%, close to the lower limits of typical melanomas. These high values may direct a patient’s management to close monitoring for possible recurrence. It was also shown that an increase in MIB-1/Ki-67 labeling index observed in recurrent lesions indicates melanocytoma malignant transformation (19,24).

IGMs were speculated to have a more aggressive clinical behavior than meningeal melanocytomas despite the small number of lesions reported to date. In 16 patients with IGM up
to date, patient age ranged from 17 to 79 years (5,8,9,11,13,16–20,22,24–28). Our patient was 19-month-old—the first reported patient with IGM in childhood. Different treatment modalities were employed for the 16 patients presented in this study. Among the patients with no adjuvant radiotherapy, seven cases underwent total resection, five of which had recurrence; partial resection was performed in seven cases, five of which had recurrence. Of the remaining two patients who received adjuvant radiotherapy, one patient underwent total resection, while the other underwent partial resection; none had recurrence (Table I). Based on a limited number of patients, it is difficult to conclude regarding the effectiveness of different treatment modalities. These tumors tend to recur (11 of 16 patients in total), which mandated a complete surgical resection when feasible. However, achieving complete resection in their favorite locations (spinal cord and posterior fossa) is difficult (27). Recurrence was reported in 10 (71%) of 14 patients with no adjuvant treatment. No recurrence was reported in two patients with adjuvant radiotherapy. Regarding our patient, radiotherapy was not an option for a 19-month-old child, given its side effects on the developing brain. Supratentorial and convexity locations in our patient made total resection possible, and close follow-up seemed logical. This management has been successful up to now, without recurrence at 48-month follow-up.

Despite being rare, the congenital defect of parietal bones has been described either alone or together with other developmental anomalies in previous studies (6), and as part of syndromic diseases (7). They are classified into three different categories: Cranioschisis, which is a large skull defect associated with brain anomalies and incompatible with life; cranial dysostosis, which is a small bone defect in parietal bones; and foramina parietalia permagna, which is a foramen in the parietal bone exceeding 5 mm in diameter (6). ALX-4 and MSX-2 are two homeobox genes associated with skull ossification. Their haploinsufficiency is suggested to cause skull ossification defects, mostly related to foramina parietalia permagna (6). Cranial dysostosis represents a small bony defect in parietal bones relevant to our patient, which was included in preoperative differential diagnosis due to her gait difficulties and bilateral inverted foot deformity. Apparent findings of a mass lesion during the surgery and diagnosis of IGM in pathological examination did not necessitate further investigation regarding skull agenesis and genetic abnormalities.

### Table I: Reported Treatment Options and Recurrences of IGMs

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total (n)</th>
<th>Age (years)</th>
<th>Recurrent lesion</th>
<th>Time to recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total resection</td>
<td>7</td>
<td>25-71</td>
<td>5</td>
<td>3-24 months</td>
</tr>
<tr>
<td>Partial resection</td>
<td>7</td>
<td>17-79</td>
<td>5</td>
<td>8-24 months</td>
</tr>
<tr>
<td>Total resection + Radiotherapy</td>
<td>1</td>
<td>56</td>
<td>0</td>
<td>none</td>
</tr>
<tr>
<td>Partial resection + Radiotherapy</td>
<td>1</td>
<td>35</td>
<td>0</td>
<td>none</td>
</tr>
</tbody>
</table>

**CONCLUSION**

IGMs constitute a very small group of melanocytic tumors of the central nervous system with different histopathological features. Their clinical behavior and best treatment options still need to be set. Moreover, there is no information about IGMs in children in previous studies. This is the first case reported in the literature for children harboring IGM; having complete resection without adjuvant therapy and recurrence at 48-month follow-up. Further data is needed to better understand IGMs’ histopathological and clinical behavior both in adults and children.

**AUTHORSHIP CONTRIBUTION**

**Study conception and design:** MS, AD  
**Data collection:** MS, OE  
**Analysis and interpretation of results:** MS, SBU, OE, AD  
**Draft manuscript preparation:** MS, AD, OE  
All authors (MS, OE, SBU, AD) reviewed the results and approved the final version of the manuscript.

**REFERENCES**


