Medulloblastoma and juvenile pilocytic astrocytoma presenting as synchronous primary brain tumors in a child

Case report

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Multiple metastatic brain tumors and multifocal primary brain tumors of a single histological type have been published in the adult and pediatric literature. However, the simultaneous occurrence of multiple primary brain tumors with different cell types is rare. Even more rare is the pediatric presentation of multiple primary brain tumors with different cell types.

The authors describe the case of an 8-year-old boy who presented with a 2-week history of progressive headache, nausea and vomiting, and imbalance. Brain MR imaging demonstrated a heterogeneously enhancing mixed solid/cystic mass of the left cerebellar hemisphere and a larger, midline, more homogeneously enhancing lesion of the superior vermis. Spinal MR imaging was unremarkable.

The patient underwent a suboccipital craniotomy and subsequent gross-total resection of both mass lesions. Pathological examination revealed the left cerebellar and superior vermal lesions to be a juvenile pilocytic astrocytoma and a medulloblastoma, respectively. The patient did well in the immediate postoperative period, was discharged home, and underwent neurooncological follow-up.

To the best of the authors’ knowledge, they describe the first known pediatric case in which a medulloblastoma and a juvenile pilocytic astrocytoma presented as synchronous primary brain tumors. They review the literature on multiple primary brain tumors with different histological characteristics and rehash potential mechanisms for their development. (DOI: 10.3171/2009.9.PEDS09211)

Key Words • medulloblastoma • juvenile pilocytic astrocytoma • synchronous primary brain tumor • pediatric brain tumor • posterior fossa tumor

Multiple metastatic brain tumors and multifocal primary brain tumors of a single histological type are common in adult and pediatric patients. However, the simultaneous occurrence of multiple primary brain tumors with different cell types occurs infrequently. These interesting conditions have been documented in the literature in the form of single case reports or small series of cases. Synchronous primary brain tumors of different cell types in the pediatric age group are even more rare.

To the best of our knowledge, we describe the first known case in which a medulloblastoma and a JPA presented as synchronous primary brain tumors in a pediatric patient. Characterization of the tumors was confirmed by histology and molecular analysis. We review theories, predisposing factors, and mechanisms underlying this phenomenon.

Case Report

History and Examination. This 8-year-old boy with a history of meningitis as an infant presented to Texas Children’s Hospital with a 2-week history of worsening morning headaches, emesis, ataxia, and fatigue. Brain MR imaging showed 2 enhancing cerebellar lesions—the larger one centered in the cerebellar superior vermis and a smaller satellite lesion located in the left cerebellar hemisphere parenchyma (Fig. 1).
The patient was neurologically intact at presentation, except for a mild ataxic gait and dysmetria of the right arm. Interestingly, he underwent a baseline CT scan of the brain (Fig. 2) as part of a meningitis work-up as an 11-month-old infant. The scan appeared to demonstrate normal findings. Even retrospective review of the imaging study showed no indication of the cerebellar mass lesions.

There was no family history of cancers at a young age.

**Operation.** The patient was placed in the prone position. His head was held in a military-tuck position in a 3-pin Mayfield head holder. Free-run facial nerve, soft-palate, and tongue electromyographic monitoring was performed together with upper- and lower-extremity somatosensory evoked potential monitoring for intraoperatively. A midline skin incision and occipital/suboccipital craniotomy were made to approach both lesions. A corticectomy in the left cerebellar hemisphere, based on intraoperative ultrasound, was used to resect the firm, well-circumscribed hemispheric tumor en bloc.

Next we turned our attention to the midline lesion. A small corticectomy through the inferior vermis was made to reach the soft but vascular tumor. This lesion was grossly different from the first tumor. A gross-total re-
section was achieved through a piecemeal suction-based resection. Intraoperative ultrasound confirmed complete resection of both lesions.

Pathological Examination. The left cerebellar tumor showed typical histopathological features of a pilocytic astrocytoma (WHO Grade I, according to the 2007 classification) (Fig. 3). The biphasic tumor had predominantly solid compact areas with bipolar cells having round to oval nuclei. There were interspersed cystic areas with myxoid material containing round, process-poor cells. Many Rosenthal fibers and calcifications were noted in the compact areas. Focally round cells with perinuclear halos resembling oligodendrocytes were seen. Immunostaining with GFAP showed diffuse positivity of the tumor cells, and immunostaining with Ki 67 showed a low proliferation index of 1–2%. Chromosome analysis of a 5-day primary culture revealed a normal male karyotype with no evidence of clonal abnormality.

The paramedian cerebellar tumor exhibited a highly cellular small blue cell neoplasm (Fig. 4). The tumor cells were densely packed with a focal nodular pattern. They had hyperchromatic and pleomorphic, elongated nuclei and scant cytoplasm. There were focal pale nodules with formation of neuropil, highlighted by lack of reticulin staining. Synaptophysin was present in the pale nodules and was concordant with the neuronal differentiation that is represented in the pale nodules. Numerous mitotic figures and apoptotic bodies were seen. The GFAP immunostain demonstrated residual infiltrated neuropil and reactive astrocytes. Immunostain with Ki 67 showed a high proliferation index of 95%. A P53 immunostain showed diffuse and strong nuclear positivity in over 90% of the tumor cells. Chromosome analysis of a 7-day primary culture revealed a near-tetraploid clone with multiple structural and numerical changes in 8 of 20 cells examined: (83,XXYY, +X, add (1)(p13) x2, +9, -10, -10;der (12;?) x2, -13, -16, -16, -17, -18, -18;12;22)(q10;q10) x2, -21, +3mar[8]). A diagnosis of medulloblastoma with focal anaplasia and residual nodular pattern (WHO Grade IV [2007]) was rendered.

Postoperative Course. The postoperative course was unremarkable. The patient remained neurologically intact except for mild cerebellar signs and symptoms. Postoperative MR imaging of the brain showed no residual tumor.
At 6 months, the patient is completing treatment for medulloblastoma based on a collaborative multiinstitutional study. This treatment consists of craniospinal radiation therapy to a dose of 23.4 Gy followed by a boost to the tumor bed to a total of 55.8 Gy. He is currently undergoing chemotherapy consisting of 4 cycles of high-dose drugs followed after each course by stem cell rescue. In this protocol we do not upstage risk categorization based on degree of anaplasia. Clinical staging determines the risk categorization.

**Treatment Rationale.** There is no evidence to date that children with medulloblastoma with focal anaplasia require a different or a more intensive treatment approach. It is widely accepted that children with large cell/anaplastic medulloblastoma have a poorer prognosis and therefore require a more aggressive treatment approach. The current Children's Oncology Group trial for those with medulloblastoma who are considered to be at high risk for recurrence includes children with any degree of anaplasia, and they all receive higher doses of craniospinal radiation to 36 Gy. Future prospective studies may shed light on the correlation between the degree of anaplasia and outcome.

We did not specifically treat the child in this report for the JPA because this lesion was completely resected. In addition the area where the JPA was present received at least a dose of 23.4 Gy.

**Discussion**

Multiple synchronous brain tumors are most commonly encountered in the form of metastatic disease. The incidence of primary multiple brain tumors is much lower. These lesions are usually of the same histological type: multifocal gliomas and multiple meningiomas, schwannomas, ependymomas, teratomas, and hemangioblastomas. Synchronous germinomas and, less commonly, synchronous multicentric pleomorphic xanthoastrocytomas and JPA associated with neurofibromatosis Type I have been reported in the pediatric age group. Multiple primary brain tumors of different cell types are very rare and have been documented only in single case reports and small case series.

**TABLE 1: Different combinations of multiple intracranial tumors reported in the literature**

<table>
<thead>
<tr>
<th>First Tumor Associated Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>meningioma</td>
</tr>
<tr>
<td>glioma, oligodendroglioma,</td>
</tr>
<tr>
<td>spongioblastoma, ependymoma,</td>
</tr>
<tr>
<td>sarcoma, angiomatous tumors,</td>
</tr>
<tr>
<td>medulloblastoma, cerebellar,</td>
</tr>
<tr>
<td>acoustic neuroma, facial nerve</td>
</tr>
<tr>
<td>pituitary adenoma</td>
</tr>
<tr>
<td>oligodendroglioma, ependymoma,</td>
</tr>
<tr>
<td>meningioma, chordoma, cranial</td>
</tr>
<tr>
<td>pituitary adenoma</td>
</tr>
<tr>
<td>glioma</td>
</tr>
<tr>
<td>medulloblastoma, sarcoma, teratoma, hemangioblastoma,</td>
</tr>
<tr>
<td>choroid plexus papilloma†</td>
</tr>
<tr>
<td>subependymal giant cell astrocytoma</td>
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* Information adapted from Butti et al.
† Pediatric case described by Maria et al.

Fig. 5. Postoperative coronal Gd-enhanced T1-weighted MR image showing gross-total resection of both tumors.
Synchronous pediatric medulloblastoma and JPA

times.12 The theory did not explain why these cells remained latent for years, nor why only an occasional rest of embryonic cells developed into cancer.1

A systemic carcinogenic principle, such as Li-Fraumeni syndrome,18,36 neurocutaneous syndromes,8,24 and related syndromes linked to germline mutations of genes that normally help to control cell growth, is hypothesized to greatly increase a susceptibility to cancer. This has the potential of producing multiple intracranial neoplasms as well as tumors involving other organ systems.13 Mutations may be inherited or may arise de novo early in embryogenesis or in one of the parent’s germ cells.

Other authors6,11,20 have speculated that one of the tumors may act as an irritant, capable of stimulating the development of the other adjacent tumor. In our case, given the adjacent locations of the tumors, this theory seems plausible and more than mere coincidence.

Exposure to radiation can play an important role in the development of multiple primary brain tumors. The observation has been made that patients who receive cranial irradiation for a single brain neoplasm are at higher risk for the development of a second tumor at a later date.10,27 Trauma has also been implicated as one of the causal factors of tumorigenesis.11 Our patient has no history of radiotherapy or head trauma. On the other hand, the advent of neuroimaging is thought to be responsible for factiously increasing the incidence of multiple brain tumors by the increased presence of a surveillance artifact.11

Conclusions

As our case illustrates, two separate intracranial masses may not represent CNS dissemination of a single primary tumor. A symptomatic tumor is an indication for surgery. An asymptomatic second tumor may be followed clinically and radiographically if not reached easily through the same craniotomy at the time of first surgery, or it may be resected for definitive diagnosis, as described in this report.

The potential role of genetic factors, head injury, radiotherapy, and “irritative effect” of other adjacent tumors in the development of multiple primary brain tumors remains speculative. Tumorigenesis is likely a complex multistep process that can be influenced by tumor environment, activation of oncogenes, or the loss of tumor suppressor genes.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References


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