Teratomas constitute a group of nongerminomatous germ cell tumors that reproduce to various degrees the cellular and structural phenotypic traits associated with the three classic germ layers. These tumors account for 3% of all childhood tumors, are rarely found in the brain, and constitute 2% of all intracranial neoplasms in children younger than 15 years of age. Teratomas are classified as mature, immature, or malignant. Mature teratomas more faithfully recapitulate normal tissues, albeit in highly abnormal locations. The hallmark of immature teratomas is the conspicuous presence of cellular populations that retain an embryonal character. Frequently, these immature elements differentiate into primitive neuroepithelial structures with histopathological patterns resembling medulloepithelioma, neuroblastoma, retinoblastoma, or ependymoblastoma. In the present report, we describe the case of a 2-year-old boy with an immature teratoma of the posterior fossa that had partially differentiated into a medulloblastoma.

KEY WORDS • germ cell tumor • primitive neuroectodermal tumor • teratoma • medulloblastoma • pediatric neurosurgery

Case Report

History and Examination. This 2-year-old boy presented to his pediatrician with intermittent headaches and emesis. His recent history was notable for a worsening in motor coordination and speech. According to his parents, both of these findings represented a regression from his baseline status just 2 months prior to presentation. On physical examination, bilateral papilledema was noted, as were bilateral upward and lateral gaze palsies. Strength was normal in all extremities, but the child demonstrated marked trunk and limb ataxia. Computed tomography scanning of the brain revealed hydrocephalus and a hyperdense mass within the fourth ventricle. The presence of the fourth ventricle mass with evidence of diffuse leptomeningeal spreading was confirmed on MR imaging (Fig. 1). An MR image of the spine showed no evidence of metastatic disease.

Operation. After placement of a right frontal EVD, a posterior fossa craniotomy was performed. After the dura mater had been opened, the disseminated tumor was evident within the subarachnoid space of the dorsal surface of the cerebellum. The fourth ventricle component of the tumor
was seen to protrude through the vallecula, and the bulk of the tumor was revealed after splitting the inferior portion of the vermis. The consistency of the tumor varied from areas that were soft and easily aspirated to others that were firm and calcific. The lesion appeared to have arisen within the inferior medullary velum and was lifted easily off the floor of the fourth ventricle, which was uninvolved. The fourth ventricle component of the lesion was completely removed.

**Histological Examination.** Results of a histopathological examination of the fourth ventricle lesion revealed a fragmented mass consisting of tubular structures that resembled primitive neural tubes positioned adjacent to nests of hepatoid differentiation. Areas of intestinal mucosa and glial differentiation were also noted, as were areas composed of immature cartilage, adipose tissue, and striated muscle. Admixed into this larger mass was an area of small malignant-looking blue cells with large pleomorphic hyperchromatic nuclei and scant cytoplasm arranged in sheets (Fig. 2). Mitotic cells were readily identified. Immunohistochemical analysis demonstrated diffuse staining of the small blue cells with synaptophysin and nuclear staining for the epithelial component of BAF47. The BAF47 antibody is a marker for the nuclear tumor suppressor gene \( \text{INI1} \), a member of a chromatin remodeling complex that is lost in atypical teratoid/rhabdoid tumors but retained in medulloblastoma.\(^8\) The neural tubes stained positively for CAM 5.2, and the hepatoid component for \( \alpha \)-fetoprotein. Stains for placental alkaline phosphatase and \( \beta \)-human chorionic gonadotropin were both negative, indicating the absence of a malignant germ cell component. These findings were consistent with the diagnosis of immature teratoma with partial differentiation into medulloblastoma.\(^2,5,16\) A tumor sample removed from the subarachnoid space was also found to be histologically consistent with medulloblastoma. Fluorescence in situ hybridization demonstrated no deletion in the region of 22q11.2, excluding the diagnosis of an atypical teratoid/rhabdoid tumor.\(^9\)

**Postoperative Course.** After the surgery, extubation was accomplished and the patient’s neurological status was the same as it was preoperatively. An MR image obtained on postoperative Day 1 showed no evidence of residual tumor within the fourth ventricle; however, diffuse and predominantly infratentorial disease was again noted (Fig. 3 left). Over the next several days the patient’s headaches and ophthalmoplegia improved and he tolerated removal of the EVD. Approximately 10 days postsurgery, chemotherapy was initiated using a Head Start III regimen of cisplatin, vincristine, cyclophosphamide, and etoposide. The patient’s neurological status continued to improve until postoperative Day 14, at which time his condition abruptly deteriorated. Computed tomography scanning of the brain demonstrated hydrocephalus with obstruction of the fourth ventricle and basal cisterns, and an MR image showed a dramatic worsening in the extent of leptomeningeal dissemination as well as a small recurrence within the fourth ventricle (Fig. 3 right). The patient’s condition stabilized after placement of an EVD, but 2 days later his neurological status again worsened. Repeated imaging revealed further compression of the posterior fossa structures and filling of all the cisterns within the posterior fossa with tumor. On postoperative Day 17, the patient underwent surgery for posterior fossa decompression. A biopsy sample obtained from the tumor within the subarachnoid space yielded results consistent with medulloblastoma. Salvage chemotherapy with methotrexate was considered, but in accordance with his family’s wishes, he was discharged home with hospice care. The child died approximately 1 week later.

**Discussion**

Teratomas are a group of nongerminomatous germ cell tumors composed of a mixture of well-differentiated tissues of the adult type derived from all three germinal cell layers, accounting for 2% of all intracranial tumors in children.
younger than the age of 15 years. Intracranial teratomas mimic other intracranial germ cell tumors in their proclivity for the midline, most often arising in the pineal gland and suprasellar region, followed by the regions of the third and fourth ventricles. The World Health Organization classification of intracranial teratoma delineates three histological variants: mature, immature, and malignant. Mature teratomas often fulfill the classic expectations of their name, displaying well-differentiated tissue types of ectodermal, mesodermal, and endodermal origins. If the lesion is completely excised, patients with mature teratomas have a good prognosis, with a reported 10-year survival rate greater than 90%. The prognosis is significantly worse for patients with immature and malignant teratomas, with a 10-year survival rate of 70% and a 5-year survival rate of less than 50%, respectively. The hallmark of immature teratomas is the presence of cellular populations that retain an embryonal or fetal character; these cell populations may occasionally give rise to cancers of a somatic type. Occasionally, immature and malignant teratomas give rise to neuroepithelial structures with histopathological patterns resembling medulloblastoma, neuroblastoma, retinoblastoma, or ependymoblastoma. To our knowledge, this is the first report of a case of immature teratoma of the central nervous system that partially differentiated into a medulloblastoma.

Medulloblastoma is the most common posterior fossa tumor in children. This lesion often arises from the cerebellar hemispheres adjacent to the midline, deep to the cerebellar vermis, and extends caudally toward the foramen magnum and ventrally toward the floor of the fourth ventricle. Children with medulloblastoma frequently present with signs of cerebellar dysfunction, brainstem compression, and obstructive hydrocephalus. Although these lesions often seem well circumscribed, by the time they are discovered they have often become microscopically invasive. In our experience, in nearly one third of children presenting with medulloblastoma there is evidence of leptomeningeal spread of disease at the time of the diagnosis (T. Tomita, personal communication). Although the goal of surgery is complete resection, the survival benefit of gross-total resection in high-risk children (those <3 years of age or with evidence of cerebrospinal dissemination at initial presentation) remains unclear.

Recent data support the hypothesis that medulloblastoma...
mas arise from the disturbance of pathways involved in external granule cell development. Authors of other studies have reported finding mature cerebellar tissue within teratomas located outside the central nervous system axis, which suggests that some of the progenitor cell and molecular cues necessary for cerebellar differentiation were available. It is possible that the process of cerebellar differentiation in our patient was disrupted by the genetic makeup of the underlying germ cell substrate, creating the conditions that gave rise instead to a medulloblastoma.

References


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