Brief Communication

Immature Teratoma of the Leptomeninges in an 8-Year-Old Child: Unusual Presentation With Recurrent Transient Oculomotor Nerve Palsies and Rapid Progression to Diffuse Brain Infarction

The brain is one of the extra-gonadal sites in which germ cell tumors may develop. These intracranial tumors usually present in the second or third decade of life and occur in midline brain locations, most frequently in the suprasellar or pineal regions, or both, with symptoms referable to these locations.[1-4] Intracranial germ cell tumors also have metastatic potential and frequently disseminate through cerebrospinal fluid pathways to ventricular and leptomeningeal surfaces at diagnosis or at the time of relapse. Primary involvement of the leptomeninges by these tumors, until now, was unknown.

We report a previously undescribed clinical presentation in a child who was proven at autopsy to have an immature teratoma that diffusely involved all leptomeningeal surfaces of brain without evidence of parenchymal tumor. Her unusual presentation consisted of initial pulsatile recurrent headaches, followed by brief, transient, and recurrent oculomotor nerve palsies with rapid progression to irreversible diffuse cerebral ischemia and brain death within 36 hours.

Case Report

An 8-year-old girl had been well until 1 week before presentation when she had new onset of intermittent bifrontal pulsatile headaches. She was admitted to an outside hospital when they became more frequent, severe, and associated with nausea and vomiting. An initial computed tomographic (CT) brain scan was normal except for very slightly prominent ventricles. Lumbar cerebrospinal fluid cell count was 1 white blood cell, 0 red blood cells, glucose and protein content were normal, and Gram stain and cultures were negative for routine bacteria and acid-fast bacilli. Shortly after her transfer to our institution for further evaluation, 9 days into the illness, she had a 10 to 15 minute episode of transient right hemiparesis and expressive dysphasia that led to an initial presumptive diagnosis of complicated migraine headache. High-dose corticosteroids (2 mg/kg/day prednisone) were given as treatment for status migrainosis. Brain magnetic resonance imaging (MRI) showed diffuse enhancement of the leptomeninges, more prominent and nodular-appearing near the vein of Galen and midbrain (Figure 1). During the next 36 hours the child had 5 episodes of acute intermittent, complete oculomotor nerve palsies. Some were unilateral and some were bilateral, and each episode resolved completely within 30 minutes. CT imaging repeated during one of the episodes was unchanged. However, following the sixth such episode, she became lethargic and progressively unresponsive. Over the next 2 hours, brainstem reflexes disappeared, motor signs progressed from decerebrate posturing to absent responses, and her examination became consistent with brain death. A CT scan done early during that period showed changes consistent with diffuse cerebral ischemia, with initial sparing of diencephalon and cerebellum and no cerebral herniation. She was treated for increased intracranial pressure with hyperventilation and mannitol but had further neurologic deterioration with loss of all brainstem reflexes and motor responses. Increased cerebral edema had resulted in cerebral herniation evident on repeat CT imaging.

At autopsy, the brain was markedly edematous with diffuse leptomeningeal opacity. Microscopically, a thin layer of immature teratoma within the subarachnoid space encased the entire brain (Figure 2A). No tumor was identified in brain parenchyma except in Virchow-Robin spaces around superficial vessels in a few brain regions, and no systemic tumor was identified. The pineal gland showed reactive gliosis with numerous Rosenthal fibers, but no neoplasm (Figure 2B). Diffuse ischemic changes were present in brain parenchyma. The diagnosis of teratoma was made on the presence of elements representative of all three germ cell layers (Figures 2C and 2D). The components of immature neuroepithelial structures such as medulloepithelioma, as well as other malignant epithelial structures qualified this tumor as immature or malignant teratoma (Figure 2D). The diagnosis was confirmed by stains that were positive for CAM 5.2, alpha-

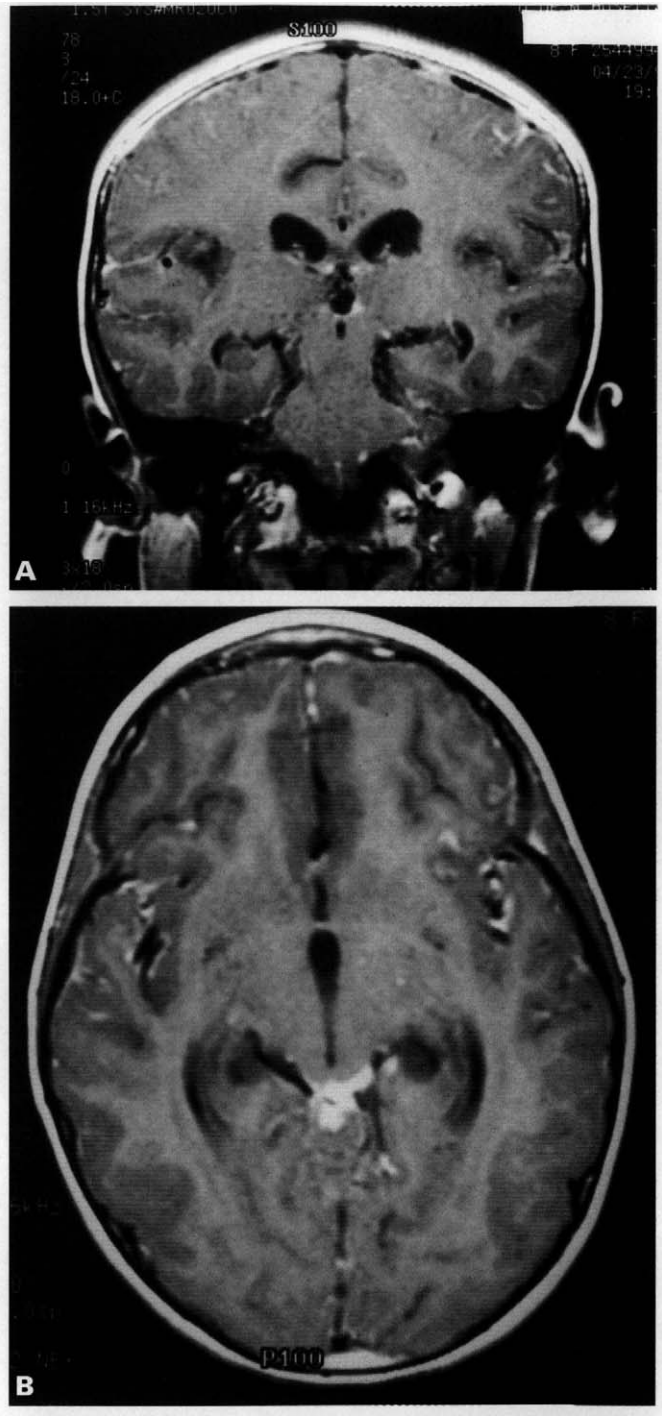

Figure 1. *A*, Coronal T_1-weighted MRI of brain after gadolinium administration illustrating diffuse enhancement of the leptomeninges over cerebral convexities, brainstem, and Sylvian fissures. *B*, T_1-weighted axial image illustrating gadolinium enhancement most prominent in the region of the vein of Galen and superior colliculus.

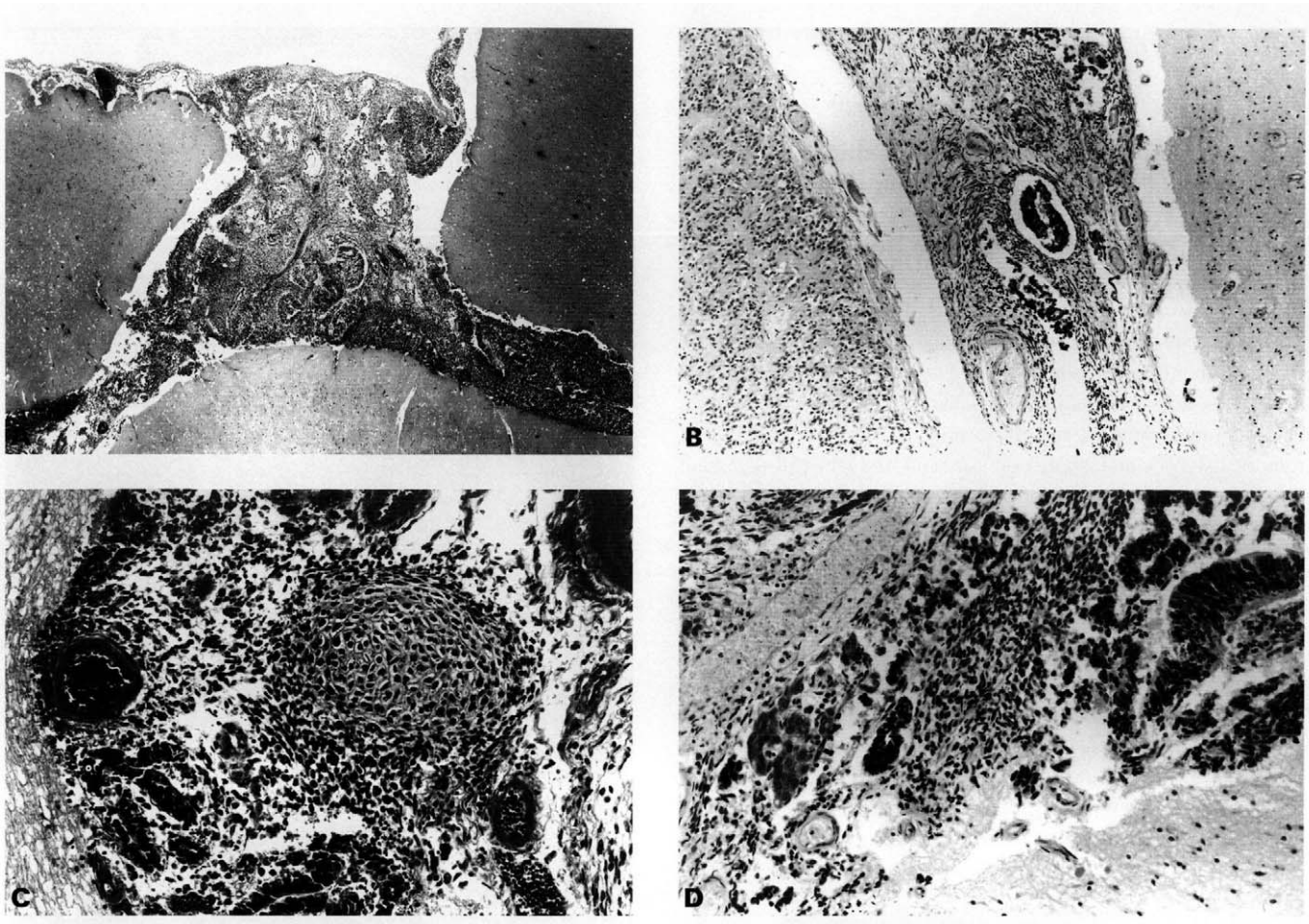

Figure 2. Photomicrographs of autopsy sections of brain and tumor stained with hematoxylin and eosin. *A,* Illustration of portions of brain gyri on left, right, and bottom covered and encased but not invaded by neoplasm. (Original magnification ×29.8). *B,* Illustration of meningeal neoplasm (center) between pineal gland with gliosis on the left and cortical brain on the right. (Original magnification ×58.75). *C* and *D,* Portions of the neoplasm illustrating tissues derived from all three germ cell layers, *C,* cartilage (center), mesenchymal cells (upper left), and glandular epithelium (lower left) and *D,* endothelium in vessels (upper left), mesenchymal cells (center), and immature neuroepithelial tissue (right), adjacent to brain on the bottom. (Original magnification, ×235).

fetoprotein, and vimentin in regions corresponding to various lines of differentiation. The poorly differentiated portion of the tumor, which accounted for the majority of it, was negative for all these stains as well as for glial fibrillary acidic protein, synaptophysin, beta-human chorionic gonadotropin, and Ber-H_3 (an embryonal carcinoma marker).

Discussion

Two aspects of this case were unusual. The first was the previously undescribed location of this immature teratoma involving the leptomeninges with no evidence of parenchymal brain or systemic tumor. The second was the remarkable clinical presentation of this neoplasm, with its short course, development of frequent, transient, and reversible third nerve palsies and ultimately, rapid progression to brain death from diffuse brain ischemia.

The immature or malignant teratoma diagnosed in this case is one of several inter-related but histologically diverse neoplasms of germ cell derivation that are classified into germinoma or nongerminoma variants. The central nervous system is just one of several extragonadal sites of origin of these germinal tumors.[1] Immature teratomas belong to the non-germinoma group, which also includes embryonal carcinoma, endodermal sinus tumor, and choriocarcinoma.[3] The diagnosis of immature teratoma in this case was made on the presence of tissue representative of all three germ cell layers, but with the majority of the neoplasm having features of malignant embryonal neuroepithelial tissue including ependymoblastoma and medulloepithelioma.[5] The diagnosis was confirmed by immunoperoxidase stains that demonstrated poor differentiation of the neural component.

As a group, germ cell neoplasms are rare central nervous system tumors, constituting fewer than 3% of brain tumors in children and young adults from North American series.[4] Their peak age of incidence is in the second and third decade of life, although some of the nongerminoma variants including the immature teratoma are more likely than germinoma to be diagnosed in infants and younger children.[4] Intracranial germ cell tumors arise predominantly (85%) in two midline locations of the central nervous system, the pineal and the suprasellar regions, or simultaneously in both.[4] The rest occur in other midline locations but occasionally off midline, in cerebral hemispheres or in lateral ventricles.[4,6–8] Through their proximity to the ventricular system, intracranial germ cell tumors frequently give rise to ventricular or craniospinal leptomeningeal metastases, either at diagnosis or at relapse.[9] However, neither immature teratoma nor any other type of intracranial germ cell tumor has previously been reported to occur in the leptomeninges exclusive of any primary parenchymal tumor, as seen in this child. It is possible

that this tumor originated in the pineal region where there were the changes of marked gliosis with abundant Rosenthal fibers, although no neoplasm was identified there.

Neoplastic leptomeningeal disease can be metastatic from systemic solid or hematologic malignancies or from primary brain tumors. Central nervous system tumors that originate in the leptomeninges are uncommon. Primary leptomeningeal gliomatosis is a rare condition attributed to malignant transformation of heterotopic neuroglial tissue diffusely in the meninges, and reported almost exclusively in adult patients.[10–14] Its presentation with headache, hydrocephalus, cranial nerve palsies, cerebrospinal fluid pleocytosis, and hypoglycorrhachia suggested a diagnosis of chronic basilar meningitis until positive cerebrospinal fluid cytology or meningeal biopsy made the diagnosis of neoplasm in these cases. In children, three cases of primitive neuroectodermal tumors that primarily involved the leptomeninges with no evidence of a parenchymal tumor, were reported.[15–17] Those cases also presented with cerebrospinal fluid pleocytosis, nuchal rigidity, and irritability resembling an infectious meningitis, until the diagnosis of leptomeningeal primitive neuroectodermal tumors was made by positive cerebrospinal fluid cytology or meningeal biopsy.

The initial clinical presentation of isolated vascular-like headaches in this child, along with the absence of cerebrospinal fluid pleocytosis or hypoglycorrhacia, was not as strongly suggestive of an infectious meningitis as were the above-described cases of meningeal gliomatosis or primitive neuroectodermal tumor. When the cranial nerve deficits developed and meningeal enhancement was seen on MRI, this diagnosis became a more serious consideration, as did other noninfectious causes of meningeal inflammation including neoplastic meningitis. Other rare etiologies of symptomatic meningeal enhancement in the differential diagnosis included sarcoidosis, meningioangiomatosis, metabolic disorders, toxins, and subarachnoid hemorrhage.[18,19] The subsequent clinical course was so rapid, however, that diagnostic measures were not completed before the child deteriorated and died. This tumor, with its extremely rapid clinical course and extensive spread at presentation, behaved more aggressively than the usual immature intracranial teratoma in a typical location. This could have been a function of more malignant intrinsic biologic behavior of the tumor, but the rapidly deteriorating course also noted in several of the primary leptomeningeal primitive neuroectodermal tumors described above, suggest that location could be a significant factor in the rapid presentation.[16,17]

The pathophysiologic mechanism of the initially transient and recurrent oculomotor nerve palsies in this child seems most likely to have had a vascular basis. The possibility of acute increased intracranial pressure causing uncal herniation was eliminated by the CT findings without evidence of this during the episodes. Direct involvement of oculomotor nerves by the neoplasm could not account for the intermittent nature of the deficits. The acute and transient deficits in a child with pulsatile headaches initially made complicated migraine seem to be a reasonable diagnostic possibility, although the ultimate course was not consistent with this. The terminal events confirmed both by CT imaging and at autopsy, also appeared to have a vascular basis, with diffuse ischemia leading to brain infarction. We hypothesize that the very unusual course in this child was due to a vaso-occlusive process. This could have resulted from direct tumor infiltration of blood vessels, although we could not confirm this at autopsy. More likely, especially given the intermittent nature of the initial ischemic deficits, it was caused by tumor-induced vasospasm that was ultimately intense and sustained.

Patricia L. Robertson, MD
Departments of Neurology and Pediatrics
The University of Michigan Medical Center
Ann Arbor, Michigan
Ivan Pavkovic, MD
Department of Neurology
Creighton University School of Medicine
Omaha, Nebraska
Charles Donovan, MD
Department of Radiology
Duke University Medical Center
Durham, North Carolina
Mila Blaivas, MD
Department of Pathology
The University of Michigan Medical Center
Ann Arbor, Michigan

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