Primary Meningeal Rhabdomyosarcoma in a Child With Hypomelanosis of Ito

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- Intracranial rhabdomyosarcomas are rare neoplasms, and those thought to be primary meningeal tumors are even more rare. Hypomelanosis of Ito is a neurocutaneous disorder believed to involve a defect in cells of neural crest origin. We report the case of a 15-month-old boy with hypomelanosis of Ito who developed a primary meningeal rhabdomyosarcoma. The patient initially presented with hydrocephalus and 2 months later developed neurologic signs localizing to the spinal cord. Radiologic studies revealed widespread leptomeningeal enhancement with compression of the spinal cord at C5-C7. A brain biopsy revealed a tumor diffusely involving the meninges. Microscopically, the tumor was composed of rhabdomyoblasts, many of which showed prominent cross-striations on routine hematoxylin-eosin staining. To the best of our knowledge, this is the first reported case of meningeal rhabdomyosarcoma in a patient with hypomelanosis of Ito and the fourth reported case of a primary meningeal rhabdomyosarcoma reported in the world literature.

**MORPHOLOGIC METHODS**

For histology, sections from formalin-fixed, paraaffin-embedded tissue were cut at 5 μm and stained with hematoxylin-eosin. Immunoperoxidase stains were performed using the avidin-biotin-peroxidase method and included antibodies to vimentin (1:600; Dako Corporation, Carpinteria, Calif) and muscle-specific actin (HHF 35; 1:50; Dakopatts A/S, Glostrup, Denmark).

**PATHOLOGIC FINDINGS**

The surgical specimen consisted of 2 fragments of pink-tan brain tissue, each measuring 1.0 × 0.7 × 0.5 cm. The specimen resembled normal brain and had no grossly identifiable tumor. Hematoxylin-eosin–stained sections revealed that the meninges were diffusely infiltrated by a neoplasm consisting of spindle cells with abundant, strongly eosinophilic cytoplasm (Figure 2, A). Overall, the tumor spared the adjacent brain parenchyma (Figure 2, B), although rare individual tumor cells were found to extend into adjacent brain substance. The nuclei within the tumor cells were peripherally located, hyperchromatic, and highly variable in size and shape. The cell shapes varied from round to “ribbonlike,” and cross-striations were easily identified in numerous cells on hematoxylin-

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Figure 1. A, Magnetic resonance imaging of the spine revealed thick, nodular, leptomeningeal enhancement on T1-weighted images. The leptomeningeal thickening exerted a mass effect on the spinal cord in the cervical region (arrow). B, Magnetic resonance imaging of the head showed dilated ventricles and nodular leptomeningeal enhancement (arrow) throughout the subarachnoid space, including the sulci around the brain, the basilar cisterns, and the sylvian fissures.

Figure 2. A, Low-power view showing the meninges diffusely infiltrated by neoplastic spindle-shaped cells with abundant eosinophilic cytoplasm containing cross-striations and immunoreactivity for muscle-specific actin, a diagnosis of embryonal rhabdomyosarcoma was made.

COMMENT

Primary rhabdomyosarcoma involving the meninges is extremely rare; only 3 cases have been reported to date.6,9,10 We report here a fourth case of primary meningeal rhabdomyosarcoma. The tumor arose in a 15-month-old child with hypomelanosis of Ito and showed diffuse infiltration of the leptomeninges, with a mass effect on the spinal cord at the C5-C7 level. The pattern of diffuse involvement of the meninges was similar to 2 of the other reported cases.9,10 In both of these cases, the presenting symptom was increased intracranial pressure with hydrocephalus, eosin-stained sections (Figure 3). Immunohistochemical stains demonstrated strong immunoreactivity for vimentin and muscle-specific actin within the tumor cells. Based on the presence of numerous strap cells with abundant eosinophilic cytoplasm containing cross-striations and immunoreactivity for muscle-specific actin, a diagnosis of embryonal rhabdomyosarcoma was made.
which was the presenting symptom in the current case. In all of the cases with diffuse involvement, the diagnosis was delayed by the inability to visualize the tumor as a discrete mass radiologically and by the absence of localizing signs clinically. This delay in diagnosis resulted in a delay of treatment in all of these cases. In the previous cases, the patients died within a few months of the diagnosis. The clinical outcome of the current case remains to be seen, as only 1 month has passed since the institution of radiation therapy. In contrast to the cases with diffuse involvement of the meninges, the third reported case of primary meningeal rhabdomyosarcoma presented as a more typical brain tumor with symptoms of headache, memory disturbances, and visual disturbances. A discrete mass lesion involving the right falcotentorial region was identified and resected. This patient has had recurrences, but was alive 3 years after the initial diagnosis. The clinical outcomes of these 3 cases suggest that the finding of diffuse involvement of the meninges, termed primary meningeal rhabdomyosarcoma by Smith et al,\textsuperscript{10} is a very poor prognostic sign. However, with the small number of reported cases, the clinical behavior of these primary meningeal tumors will likely remain unclear.

Equally unclear is the histogenesis of intracranial sarcomas and particularly rhabdomyosarcomas. The meninges have both mesenchymal and neuroectodermal origins and thus may contain pluripotent mesenchymal cells.\textsuperscript{10} This feature has been proposed as the explanation for the occurrence of various sarcomas as primary tumors arising from the meninges.\textsuperscript{10} It is interesting, however, that a primary intracranial rhabdomyosarcoma involving the meninges is more likely to have arisen from the brain substance with extension into the adjacent meninges than to have arisen in the meninges de novo.\textsuperscript{3,10} This suggests that the cell origin of an intracranial rhabdomyosarcoma is either present in greater numbers or is more easily transformed within the brain substance compared to the meninges. An alternate possibility is that transformed pluripotential mesenchymal cells are induced to differentiate along rhabdomyoblastic lines within the brain parenchyma, but not within the meninges.

From a more practical standpoint, this case is instructive to the practicing surgical pathologist. When one encounters a patient with hydrocephalus with or without diffuse meningeal enhancement on radiologic studies, meningeal sarcomatosis should be considered in the differential diagnosis. A positive cerebrospinal fluid cytology may be helpful, although the cerebrospinal fluid was surprisingly devoid of tumor cells in one of the other reported cases of meningeal rhabdomyosarcoma,\textsuperscript{9} as well as in the case reported here. A meningeal sarcoma may originate from the meninges as a primary neoplasm or extend into the meninges from adjacent brain or soft tissue primary sarcoma. Metastases of sarcomas to the meninges from a remote site rarely, if ever, occur.\textsuperscript{12} Other tumors that should be considered in the differential diagnosis of a meningeal sarcoma with myoblastic features include medullomyoblastoma and teratoma. These neoplasms can have myoblastic elements that can be confused with a rhabdomyosarcoma. The absence of neuroblastic elements and heterologous elements helps to distinguish a rhabdomyosarcoma from these other tumors. The classification of a tumor as a primary meningeal sarcoma depends exclusively on radiologic and clinical findings. It is impossible to distinguish a primary from a secondary neoplasm on histologic grounds.

Rhabdomyosarcoma has been associated with several congenital disorders, including neurofibromatosis\textsuperscript{13} and Gorlin basal cell nevus syndrome.\textsuperscript{14} Interestingly, our patient has a diagnosis of hypomelanosis of Ito, a genetic neurocutaneous disorder characterized by hypopigmented lesions and congenital anomalies of the nervous system, musculoskeletal system, or both.\textsuperscript{11} Although the pathogenesis of hypomelanosis of Ito is not fully understood, it is considered a disorder of neural crest cell migration, one of the so-called neurocristopathies.\textsuperscript{11} Embryologically, the neural crest gives rise to neural elements, but also may give rise to some mesenchymal elements in the head and neck.\textsuperscript{10} Included within the group of malignant neoplasms with mesenchymatous differentiation that can occur within the central nervous system or head and neck are the medullomyoblastoma and ectomesenchymoma (gangliorhabdomyosarcoma). Both of these neoplasms contain cells with both neuroepithelial and rhabdomyoblastic differentiation, and it has been postulated that they may arise from neural crest elements.\textsuperscript{15} The rhabdomyosarcoma described in this case report had no evidence of neuroepithelial differentiation on hematoxylin-eosin-stained sections. Unfortunately, insufficient tumor was available to perform additional stains for neuroepithelial or neural crest markers. It is known that one of the tissues with a mixture of mesenchymal and neural crest elements is the meninges. Therefore, it is intriguing to consider the possibility that a defect in neural crest development played a role in the pathogenesis of both hypomelanosis of Ito and meningeal rhabdomyosarcoma in this case. However, given the small number of cases of primary intracranial rhabdomyosarcoma reported in the world literature, it would be difficult to prove the association exists.

In conclusion, a primary meningeal rhabdomyosarcoma should be considered in the differential diagnosis of central nervous system sarcomas. In the case reported here, there was no clinical or radiologic evidence of a primary neoplasm outside the meninges. Therefore, this tumor is best classified as a primary meningeal rhabdomyosarcoma, embryonal type, well differentiated. To the best of our knowledge, this case represents the fourth case of a primary meningeal rhabdomyosarcoma and the first case associated with hypomelanosis of Ito reported in the medical literature.
References