Malignant fibrous histiocytoma of the meninges

Histological, ultrastructural, and immunocytochemical studies

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A case of malignant fibrous histiocytoma arising from the meninges in a 12-year-old boy is reported. This tumor presented as an extracerebral hemorrhagic mass in the left frontal lobe without obvious invasion of the underlying brain. Histologically, a malignant tumor with the characteristic storiform pattern of malignant fibrous histiocytoma with focal areas of hemorrhage was observed. Ultrastructurally, fibroblastic cells, undifferentiated cells, histiocytic-type cells, multinucleated tumor giant cells, and xanthomatous cells were distinctly seen. The possible cell of origin of these meningeal tumors and their prognosis are discussed. The significance of considering this entity in the differential diagnosis of those tumors of the central nervous system with a spindle-cell or xanthomatous component is discussed, and the value of ultrastructural and immunocytochemical study with glial fibrillary acidic protein in the diagnosis is stressed.

KEY WORDS • malignant fibrous histiocytoma • meningeal tumor • xanthomatous tumor • ultrastructural study • glial fibrillary acidic protein

Malignant fibrous histiocytoma (MFH) is a pleomorphic sarcoma of deep soft tissue in adults. Different terminologies including “malignant fibrous xanthoma,” “xanthosarcoma,” and “fibroxanthosarcoma” are also used to describe this entity. Meningeal MFH is rare, and thus far only four cases have been recorded. Three of these cases were of primary origin from the meninges and the fourth occurred in the meninges in a patient several years following irradiation for a pituitary adenoma. A few cases that were originally reported to be MFH of the meninges have subsequently been found to be gliohistiocytomas by immunocytochemical studies. In this communication, we report a case of MFH in a 12-year-old boy, arising primarily from the meninges, with documentation by light microscopic, ultrastructural, and immunocytochemical studies with glial fibrillary acidic protein (GFAP). Areas of hemorrhage were an unusual feature of this tumor.

Case Report

This 12-year-old right-handed white boy was brought to the emergency room with sudden onset of right hemiplegia and aphasia. He apparently came home after playing football unable to speak or use his right arm, but able to walk. The right arm subsequently became densely paralyzed. Past history was significant in that, 3 to 4 months prior to the present episode, he had two episodes of jerking eye movements to the right and possibly adversive head movements to the right, suggestive of focal seizures.

Examination. He was an alert child with dense right hemiplegia and global aphasia. The fundi were normal. He was hyperreflexic on the right with a Babinski response. Investigations revealed normal laboratory data, x-ray films of the chest and skull, and electrocardiogram. Computerized tomographic (CT) scan of the head showed a large mass lesion in the left frontal lobe above the lateral ventricles with an adjacent area of enhancement suggestive of hematoma, neoplasm, or arteriovenous malformation (Fig. 1). Radionuclide brain scan showed an area of increased uptake in the left frontoparietal region compatible with a neoplasm. Left carotid arteriogram identified a high left frontal vascular mass. The patient underwent craniotomy, and a large vascular 6-cm tumor mass with an underlying hematoma was encountered on opening the
The tumor was almost completely resected. The underlying brain was apparently normal.

**Light Microscopy.** Several pieces of hemorrhagic and tan-colored tumor tissue were sent for histological examination. The hematoxylin and eosin-stained sections from formalin-fixed tissue revealed a very highly cellular and pleomorphic tumor with a small piece of underlying brain tissue. Mostly, the tumor had a characteristic storiform pattern and was composed of plump spindle-shaped cells arranged in a cartwheel fashion around small blood vessels. Plump spindle-shaped cells often consisted of either a fibroblastic or a histiocytic type of cell. The fibroblastic cells were frequently elongated with marked variation in the nuclei. The histiocytic cells often had bizarre, pleomorphic nuclei with foamy vacuolated or opaque acidophilic cytoplasm. Multinucleated tumor giant cells and Touton type of giant cells were present in moderate numbers (Fig. 2). Foamy xanthomatous cells were also observed. Gordon-Sweet's reticulin stain demonstrated increased reticulin as well as the characteristic pattern of the reticulin fibers (Fig. 3). Phosphotungstic acid-hematoxylin (PTAH) stains for the glial fibers were negative. No cross striations were demonstrated in the spindle or the giant cells with routine PTAH stains. Atypical mitoses and bizarre forms were a conspicuous feature. Multiple areas of hemorrhage with small cystic areas resulting from the absorption of these hemorrhages, hemosiderin-filled macrophages, and numerous endothelial-lined blood vessels were also prominent. The underlying brain tissue showed focal islands of spindle-shaped cells with some astrocytic response in the adjoining tissue. The intervening brain tissue was otherwise free of tumor. The Virchow-Robin spaces around the blood vessels also contained tumor cells (Fig. 4).
Malignant fibrous histiocytoma of the meninges

**Electron Microscopy.** Glutaraldehyde-fixed tumor tissue was postfixed in osmium tetroxide (OsO₄) and processed for electron microscopy. Ultrastructural studies were performed using a JEM 100c transmission electron microscope. Toluidine blue-stained thick sections revealed spindle-shaped and multinucleated cells. Ultrastructurally, five different cell types were identified: 1) fibroblastic type of cells; 2) immature undifferentiated cells; 3) xanthomatous cells; 4) a histiocytic type of cell; and 5) multinucleated tumor giant cells. The fibroblastic type of cells often had elongated nuclei with one or more nucleoli (Fig. 5). Nuclear envelopes frequently showed invaginations. The cytoplasmic organelles consisted of abundant rough endoplasmic reticulum (RER), well developed Golgi apparatus, mitochondria, and occasional lipid droplets. Many of the cells had an attenuated cytoplasmic projection. The immature undifferentiated cells often had a smooth surface, many free ribosomes, RER, and Golgi elements. Examination of the xanthomatous cells showed the presence of numerous lipid droplets either as empty spaces or electron-dense homogeneous material within the cytoplasm. The histiocytic cells characteristically had a ruffled cell membrane (Fig. 6). Most often, the nuclei were oval with slight wavy outlines, and the cytoplasm had abundant smooth and rough endoplasmic reticulum, Golgi apparatus, and mitochondria. In addition, the tumor also contained some giant cells with more than two or three nuclei, irregular outlines, and numerous mitochondria within the cytoplasm. Many areas also showed the extreme vascular nature of the tumor and the arrangement of the tumor cells around small blood vessels.

**Immunocytochemical Staining for GFAP.** The peroxidase-antiperoxidase method of Steinberger was used on fixed paraffin-embedded tissue. Antihuman GFAP rabbit serum was used. The control sections were treated with normal rabbit serum. Both these sections gave a negative reaction, thereby indicating the nonglial origin as well as absence of a neoplastic glial component in the tumor.

**Discussion**

Among the soft-tissue sarcomas, malignant fibrous histiocytoma (MFH) or fibroxanthosarcoma has been...
recognized as being of importance only in the last few years. Even though a number of cases were described by Kauffman and Stout in 1961 and by O'Brien and Stout in 1964, it was not until 1972 that this tumor attracted the attention of many pathologists. Since then, case reports with histological subtypes have been published. Now, MFH is considered routinely in the differential diagnosis of a pleomorphic sarcoma. Electron microscopy is helpful in the diagnosis of undifferentiated soft-tissue sarcomas of various types. Histologically, MFH is characterized by plump spindle-shaped cells arranged in a cartwheel pattern around small blood vessels. Spindle-shaped cells are often composed of both fibroblastic and histiocytic types of cells, and often the latter cells have bizarre multinucleated forms. Another characteristic feature is the presence of Touton giant cells and xanthomatous cells. Reticulin stains specifically help to demonstrate the increase in the reticulin fibers as well as the characteristic pattern of these tumors. The malignant form is recognized by the increase in mitotic activity.

Fu, et al., and Taxy and Battifora have shown by electron microscopy that MFH is composed of five different types of cells, namely, fibroblastic cells, poorly differentiated or immature cells, xanthomatous cells, histiocytic-type cells, and multinucleated tumor giant cells. Using the above criteria, our case would fit the category of MFH. The initial presentation of our patient with hemorrhage points to the extreme vascularity of the tumor. There have been numerous case reports of MFH involving soft tissues, studied at both the light microscopic and ultrastructural level. In the 200 cases of MFH analyzed by Weiss and Enzinger, and the 16 cases reported by Taxy and Battifora, there is no mention of the occurrence of MFH in the brain or the meninges.

Our case is the fifth reported case of MFH of intracranial origin and the first one studied by ultrastructural and immunocytochemical techniques. Three cases of MFH of the brain and the meninges, first reported by Kepes, et al., have subsequently been proven by immunocytochemistry to be gliohistiocytomas. Subsequently, a case of intracranial MFH was reported by Gonzalez-Vitale, et al., in a 37-year-old man, 11 years after he had received radiotherapy to the sella, following partial removal of a benign pituitary adenoma. Lam and Colah later reported another case. Kepes has described two further cases of MFH of the meninges in his review of xanthomatous lesions of the central nervous system (CNS).

The origin and exact nature of the histiocytes and of histiocytic tumors in general are still obscure. It is well known that histiocytes are capable of giving rise to several proliferative disorders as well as true neoplasms. Although malignant lymphomas and histiocytosis-X have been recognized to involve the CNS, MFH is not a common tumor of the nervous system. Some authors consider that the soft-tissue MFH arises from the primitive mesenchymal cells. This would suggest that the meningeal MFH could probably...
Malignant fibrous histiocytoma of the meninges

Fig. 6. Electron micrograph of a histiocytic-type cell with the characteristic ruffled cell membrane, a somewhat kidney-shaped nucleus, abundant cytoplasm, and numerous organelles. Uranyl acetate-lead citrate, × 9000.

arise from the mesenchymal stem cells of the leptomeninges.

Tumors of meningeal origin, especially fibroblastic meningiomas, could be easily confused with MFH. Many other conditions characterized by foamy cells in the stroma should also be considered in the differential diagnosis of spindle-cell tumors. These consist of a spectrum of CNS tumors where the stromal cells could undergo a xanthomatous transformation like the arachnoidal cells in meningiomas, astrocytes in glioblastomas, and lipidization of astrocytes in xanthoastrocytomas. Meningeal sarcoma and secondary fibrosarcomatous changes in a glioblastoma are the other entities to be entertained in the differential diagnosis of those tumors with a spindle- and xanthomatous-cell component. Immunocytochemical studies using GFAP are of help in differentiating pure sarcomas from the mixed sarcomas like gliosarcoma, and from pleomorphic xanthoastrocytomas. Soft-tissue MFH seems to have a poor prognosis; however, of Kepes' two patients, one with somewhat benign histological features had a relatively good outcome after surgery, while the other patient with more malignant histological features died following a recurrence. Kepes also described another similar leptomeningeal tumor occurring in the supratentorial location in 12 patients aged 7 to 25 years old, with a long-standing history of seizures. Histologically, these resembled MFH but were positive for GFAP and the patients had a good outcome. The patient of Lam and Colah had a recurrence with an unfavorable course. Our patient had done well for 18 months after surgery followed by chemotherapy and irradiation. Only the awareness of the occurrence of this neoplasm in the CNS and the follow-up results of many documented cases will give us a better idea as to the prognosis and biological behavior of this rare tumor arising from the meninges.

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