Unusual Dural and Skull-Based Mesenchymal Neoplasms: A Report of Four Cases

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Dural and skull base mesenchymal neoplasms other than meningiomas are rare. We report four such tumors, some of which are uncommon even in nonintracranial sites, in three adults and one child. The adult tumors consisted of a synovial sarcoma of the third ventricle region in a 19-year-old woman, a leiomyoma of the suprasellar region in a 57-year-old woman, and an Epstein-Barr virus (EBV)-associated smooth muscle tumor of the cavernous sinus in a 35-year-old woman with acquired immunodeficiency syndrome (AIDS). The pediatric tumor was an EBV-associated leiomyosarcoma of the left dural transverse sinus in a 14-year-old girl with common variable immunodeficiency syndrome. All tumors were thought to be primary in their dural or skull-base locations. The two EBV-associated smooth muscle tumors in immunocompromised patients expand the locations for EBV-associated smooth muscle tumors to dural and skull-base sites, the synovial sarcoma is unique to the intracranial space, and the sellar leiomyoma represents the third reported sellar smooth muscle tumor. Hum Pathol 29:240-245. Copyright © 1998 by W.B. Saunders Company

Key words: Synovial sarcoma, Leiomyoma, Leiomyosarcoma, Epstein-Barr Virus, Sella turcica

Abbreviations: EBV, Epstein-Barr Virus; AIDS, acquired immunodeficiency syndrome; MRI, magnetic resonance imaging; HIV-1, human immunodeficiency virus-type 1.

Mesenchymal neoplasms, benign or malignant, within the intracranial space are seldom seen, but when they do occur should be classified according to criteria used for their systemic counterparts. Recently, several types of systemic mesenchymal neoplasms have undergone reassessment and nomenclature changes and others have been newly identified, such as smooth muscle tumors associated with Epstein-Barr Virus (EBV) in acquired immunodeficiency syndrome (AIDS) and immunosuppressed posttransplantation patients. The fact that these same systemic neoplasms might rarely also arise intracranially in the dura or at the base of the skull is perhaps not surprising, but has seldom been reported. We describe four unusual cranial mesenchymal neoplasms—a synovial sarcoma, two EBV-associated smooth muscle tumors in immunosuppressed patients, and a suprasellar leiomyoma to enlarge the list of differential diagnoses for dural and skull-based masses.

MATERIALS AND METHODS

Cases were obtained from the pathology files of the University of Colorado Health Sciences Center, The Children's Hospital, Denver, Colorado, and its affiliates. All tissues were fixed in 10% formalin, embedded in paraffin wax and cut at 5 to 8 microns. Immunostaining was performed using the indirect immunoperoxidase technique with alkaline phosphatase detection system. Antibodies used in this study were directed against: vimentin (monoclonal) [Immunotech, Westbrook, ME], myoglobin (polyclonal) [Signet, Dedham, MA], pan cytokeratin (AE1/AE3, monoclonal) [Signet, Dedham, MA], epithelial membrane antigen (monoclonal), factor VIII (monoclonal), desmin (monoclonal), and S100 (polyclonal), [all five from DAKO, Carpinteria, CA]. Epstein-Barr virus was detected by in situ hybridization using fluorescein-conjugated EBV-encoded RNA ribonucleic acid oligonucleotide probe followed by alkaline phosphatase conjugated antifluorescein antibody; after proteinase K digestion (DAKO, Carpinteria, CA); tissue sections were counterstained with nuclear fast red.

Case Reports

Case 1. This 19-year-old Hispanic woman presented in June of 1994 with fatigue, nausea, Bell's palsy, amenorrhea, headache, polydipsia, severe hirsutism, and an 80 pound weight gain. A magnetic resonance imaging scan (MRI) revealed a 3.5 cm tumor of the third ventricle. The sella showed slight demineralization, but no bony origin or involvement by the tumor was identified. On June 7, 1994, she underwent stereotactic biopsy and placement of a ventriculoatrial shunt. The tumor was initially felt to be a craniopharyngioma, she received 5,400 cGy of radiation, and was referred to our institution for control of her diabetes insipidus. Because of her deteriorating status, a debulking of the tumor was undertaken on October 31, 1994 via the...
transcallosal approach which revealed a hypercellular, biphasic epithelial, and spindle cell neoplasm with minimal mitotic activity. Clefts (pseudoglands) were lined by low cuboidal cells and the hypercellular, sarcomatous spindle cell component was composed of fibroblast-like cells (Fig 1A). Areas of papillary formation and collagenous bands were also present. The tumor had monotonous histological features but no areas of calcification, cystic change, woven bony trabeculae, keratin pearls, basaloid or squamous epithelium, or hypocellular fibrous stroma were identified. The tumor was strongly immunoreactive for vimentin and pancytokeratin (Fig 1B,C), focally for epithelial membrane antigen, and was negative for glial fibrillary associated protein, factor VIII, and chromogranin. A diagnosis of synovial sarcoma was made, in keeping with the identity of the histological features of this biphasic tumor with synovial sarcomas elsewhere in the body, the absence of specific histological features of either craniopharyngioma or adamantioblastoma of bone, and the lack of radiographic evidence for bony origin.

The patient continued to deteriorate and additional radiographic studies indicated the spread of the tumor throughout the subarachnoid space. No systemic primary was identified and chest radiographs were negative for tumor. The patient died on December 23, 1994; permission for autopsy was denied.

CASE 2. A 56-year-old women presented to the ophthalmology service in the Spring of 1996 when she first noted difficulties with vision in her left eye. She denied any associated headache, heat or cold intolerance or recent weight gain, but had noted a progressive lack of energy over the preceding 1 to 2 years. Before the admission she had been well and had no significant medical history and had no prior surgeries. A workup revealed mild hypothyroidism and an MRI scan showed an unusual appearing 3.2 cm sellar and suprasellar mass which enhanced heterogeneously with gadolinium (Fig 2A). A transphenoidal resection of the lesion was performed and a vascular, soft mass was removed. Intraoperatively the site of origin within the sellar was unclear; the mass readily separated from the diaphragma sellae superiorly and the dural floor inferiorly, but the dura over the medial cavernous sinus was poorly visualized. Microscopically the tumor consisted of a bland spindle-cell neoplasm composed of intersecting fascicles of cells with abundant eosinophilic cytoplasm, elongate nuclei without prominent nucleoli (Fig 2B). Occasional multinucleated cells, hemosiderin deposition, no necrosis, and very rare mitotic figures, numbering less than one per 50 high-power fields were seen. Immunohistochemical stains were strongly positive for vimentin and muscle specific actin (Fig 2B); moderate immunoreactivity for S-100 was present in the cytoplasm but not nuclei. Myoglobin, desmin, desmin, estrogen, and progesterone receptors, glial fibrillary acidic protein, epithelial membrane antigen, and pancytokeratin were not detected. In situ hybridization probes for EBV were also negative. Electron microscopy showed tumor cells to possess abundant mitochondria, pinocytosis, sparse intermediate filament and dense body formation, rare poorly-formed intercellular junctions, and focally well-developed rough endoplasmic reticulum (Fig 2D). No desmosomes or interdigitating cell membranes were found. The findings were consistent with smooth muscle.
differentiation and a diagnosis of leiomyoma was made, recognizing the difficulty in establishing the criteria for benign versus malignant smooth muscle tumors in this location.

After complete gross total surgical excision, the patient had a normal gynecologic examination and is currently alive and symptom free, 6 months postoperatively, without further treatment. An MRI scan performed 6 months postoperatively showed a small amount of residual intrasellar tissue consistent with either normal pituitary gland or residual tumor.

Case 3. A 14-year-old girl with common variable immunodeficiency syndrome who had suffered from multiple infections and had had a younger brother who died from the same disease at 18 months of age, was admitted for an evaluation of chronic sinusitis. During the evaluation she was discovered to have a dural-based mass which arose in or near the left transverse and
sigmoid dural sinuses. She underwent gross total re-
moval of the 3 cm diameter tumor which on light 
microscopy consisted of an hypercellular neoplasm 
composed of fascicles of spindle cells with moderate 
nuclear hyperchromatism, no necrosis, and up to five 
mitoses per 10 high power fields (Fig 3A). Immunohis-
tochemical staining was strongly positive for muscle 
specific actin, equivocal for vimentin, and negative for 
epithelial membrane antigen, desmin, glial fibillary 
acidic protein, and factor VIII. In situ hybridization for 
EBV was strongly positive in greater than 75% of 
neoplastic cell nuclei (Fig 3B). Electron microscopy 
showed unequivocal evidence of smooth muscle differ-
entiation with bundles of microfilaments, interspersed 
dense bodies, pinocytotic vesicles, and external lamina 
(Fig 3C). A diagnosis of primary leiomyosarcoma of 
brain associated with EBV virus was made.

The child is alive and symptom free from her 
neoplasm 21 months after gross total surgical resection.

CASE 4. The patient is a 34-year-old woman with 
seroconversion to human immunodeficiency virus 
(HIV-1) in 1993. Her first AIDS-defining illness was 

In January 1997 she presented with a 1-week 
history of right-sided sixth nerve palsy and paresthesias 
in a right V2-V3 distribution which were described as a 
pins and needles sensation. She also complained of 
recent onset of headache. Her last CD4 in December 
1996 had been 81. MRI scans showed a homogeneous, 
minimally enhancing 1.2 × 0.8 cm right cavernous 
sinus mass (Fig 4A). She was taken to surgery where the 
tumor was easily dissected away from the internal 
carotid artery, but was noted to be intimately admixed 
with the venous trabeculae. The lesion was partially 
excised. Histologically, the tumor was moderately cellular, 
homogenous, and composed of fascicles of spindled 
to plump cells without nuclear pleomorphism or promi-
nent nucleoli; neither necrosis nor mitotic activity was 
present (Fig 4B). Immunostains were positive for des-
min (Fig 4C) and muscle specific actin. In situ hybridization 
probes for EBV-RNA were positive in the majority 
of tumor nuclei. A diagnosis of EBV-associated smooth 
muscle tumor was made. Although the smooth muscle 
tumor was devoid of mitoses and would be considered a 
leiomyoma in accordance with criteria used for previ-
ously published cases of EBV-associated smooth muscle 
tumors,1 the patient has shown no improvement in her 
preoperative cranial neuropathies, and an MRI scan 4½ 
months postoperatively showed an increase in the size 
of the mass, suggesting behavior more in accordance 
with a leiomyosarcoma. She died from other intracra-
nial disease August 4, 1997; autopsy was denied.

DISCUSSION

This report details four unusual neoplasms of the 
dura and skull base, several of which appear to be the 
first reports of these tumors in this location. Three 
occurred at the base of the brain, with two arising in the 
sellar/suprasellar region (cases 1 and 2, both adults) 
and one arising in or near the dural transverse sinuses

FIGURE 3. (A) Photomicrograph of the EBV-associated leiomyosarcoma from patient 3 shows a hypercellular neoplasm composed of plump to spindled cells with increased mitotic activity (arrow). (Hematoxylin & eosin stain; Original magnification ×350.) (B) In situ hybridization probe for Epstein-Barr virus in the leiomyosarcoma from patient 3 showed strong nuclear reactivity in greater than 75% of cells. (Original magnification ×230.) (C) Electron micrograph of the EBV-associated leiomyosarcoma showed well developed myofilaments (asterisk) and the external lamina (arrow). (Original magnification ×9,900.)
Two out of the three cases were recognized intraoperatively to have definite dural attachment (cases 3 and 4) and the other was strongly suspected to have attachment to the dura of the medial cavernous sinus (case 2). The fourth arose in a skull-base site, the cavernous sinus.

Our case 1 of a synovial sarcoma in brain appears to be the first report of this neoplasm in the intracranial space. Although older reports of primary brain sarcomas in the brain used classification schemas that are no longer in use, a review of these older series also does not illustrate or describe tumors that could be reclassified as synovial sarcomas today. Although permission for autopsy was denied on our patient, no visceral primary was identified in life, chest radiograph remained negative for metastatic disease, and the tumor seemed to have originated intracranially with an epicenter in the third ventricle by radiographic studies. The cell of origin for this neoplasm in the sellar/suprasellar region is conjectural; although many cases of synovial sarcoma arise close to major synovial-containing articular structures, it is no longer believed that these tumors arise from synovium per se.

Cases 3 and 4 are examples of EBV-associated smooth muscle tumors. Smooth muscle tumors, both leiomyomas and leiomyosarcomas, arising in patients with either AIDS or posttransplantation have been described, but not, to our knowledge, in intracranial or skull-base sites. Three AIDS patients have been reported, however, who have had dural leiomyomas affecting the spinal cord. Intracranial smooth muscle tumors of any type, even those unassociated with EBV, are extremely rare, with three previously reported leiomyosarcomas. One leiomyosarcoma arose from dura mater and invaded temporal muscle, one originated near the sella turcica and, the third was located in the left ventricle. A primary leiomyoma of the sella turcica region has also been reported. These cases, however, have all occurred in adults who were not immunosuppressed. Although EBV studies were not conducted, there is no reason to suspect that any of these previously reported patients harbored EBV-associated smooth muscle tumors, nor have recent studies documented EBV in smooth muscle tumors arising in immunocompetent hosts. Our cases appear to represent the first primary EBV-associated smooth muscle tumors arising near the dura or skull base.

Case 2 is a non-EBV-associated leiomyoma in an adult, the fifth reported example of a primary intracranial smooth muscle tumor, and the third in the sellar region, as noted earlier. By light microscopic criteria alone, case 2 showed the abundant fusiform eosinophilic cytoplasm and nuclear features classic for a leiomyoma. The tumor showed immunoreactivity for muscle specific actin but not desmin; the latter does not preclude a diagnosis of leiomyoma, especially in nonuterine sites. The electron microscopic findings of only focally developed myofilament and dense body formation is also characteristic of some nonuterine smooth muscle tumors. Immunoreactivity for muscle specific
actin and electron microscopic findings of focal smooth muscle differentiation excluded a diagnosis of solitary fibrous tumor of the meninges or of solitary myofibroma of adults, several recently described entities. The few examples of somewhat histologically similar intracranial or head and neck tumors diagnosed as myofibromatosis occur in the infantile or young childhood time period, often exhibited rapid growth, and seem to represent very different clinicopathologic entities from our case.

The single other report of a benign intracranial smooth muscle tumor (leiomyoma) in the literature also arose in the sellar region. Although it was diagnosed at a time (1968) antedating immunohistochemical or electron microscopic confirmation, illustrated pictures from that case report show the typical histological features of a leiomyoma. The second sellar/suprasellar intracranial smooth muscle tumor in the literature was similar to our case 2 in that it showed virtually no mitotic activity, but was designated a leiomyosarcoma on the basis of nuclear atypia. This patient displayed a fairly indolent clinical course in that he survived at least 2 years and 8 months. This shows the difficulty in establishing criteria for benignancy versus malignancy for smooth muscle tumors in nonuterine sites. Illustrated electron micrographs are also similar to our case 2 except for apparently more abundant basal lamina and myofilament formation. This report antedated immunohistochemical analyses as well.

The origin of these four mesenchymal tumors near dura and the skull base is probably not coincidental. The three smooth muscle tumors may have arisen from smooth muscle cells in intracranial veins. Systemic leiomyosarcomas have been reported to arise in veins and our pediatric EBV-associated leiomyosarcoma involved the left transverse dural sinus whereas the other EBV-associated smooth muscle tumor arose in the cavernous sinus and was noted intraoperatively to be intimately admixed with venous trabeculae. Although dural venous sinuses themselves are composed of leaflets of fibrous dura, true veins drain into then and would provide smooth muscle cell sources for tumor origin. Also, a rich venous plexus occurs at the base of the brain near the sella turcica, which might serve as an origin for these tumors and explain why our leiomyoma (case 2), and others in the literature, have originated in the sellar region.

In summary, we report four unusual mesenchymal neoplasms in three adults and one pediatric patient to broaden the potential locations for synovial sarcomas, EBV-associated smooth muscle tumors, and non-EBV smooth muscle tumors to dural and skull-base sites.

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Note added in proof. Details of the electron microscopic features of case 3 have recently been reported in Ultra Pathol 21:301-305, 1997.

REFERENCES