Primary intracranial leiomyosarcoma

Case report

DAVID N. LOUIS, M.D., E. P. RICHARDSON, JR., M.D., G. RICHARD DICKERSIN, M.D., DEBRA A. PETRUCCI, M.D., ANDREW E. ROSENBERG, M.D., AND ROBERT G. OJEMANN, M.D.

Departments of Pathology, Neuropathology, and Neurosurgery, Massachusetts General Hospital, Boston, Massachusetts

A case of primary intracranial leiomyosarcoma is presented, with clinical, radiological, light microscopic, immunohistochemical, and ultrastructural data. The histogenesis is discussed and the literature on smooth-muscle tumors of the central nervous system is reviewed.

KEY WORDS  •  leiomyosarcoma  •  brain neoplasm  •  intraventricular tumor

Primary sarcomas of the central nervous system (CNS) are uncommon tumors. Those sarcomas that display myogenic differentiation to either striated or smooth muscle are still rarer. The majority of these tumors are rhabdomyosarcomas, but sporadic cases of benign leiomyomas, medulloblastomas with smooth-muscle differentiation, and a primary leiomyosarcoma of the dura mater have been reported. Leiomyosarcomas occasionally involve the parenchyma of the CNS, but almost exclusively as metastatic lesions. Only one previous report has described a primary leiomyosarcoma of the brain. The present report documents a second example of primary intracranial leiomyosarcoma.

Case Report

This 72-year-old right-handed white woman presented with a 4-month history of changing mental status. She complained of trouble with short-term memory and of difficulty in reading, writing, and finding words. She denied weakness, visual impairment, or nausea and vomiting, but admitted to mild bifrontal headaches and occasional lightheadedness. She had undergone a mastectomy for intraductal breast carcinoma 20 years prior to her current illness. She suffered from angina, and a basal-cell carcinoma had been removed approximately 10 years previously.

Examination. On physical examination she was alert and pleasant. She spoke with mild hesitancy. The general examination was unremarkable except for a healed left mastectomy scar. Neurological evaluation revealed that she was disoriented to the date and had a marked dysnomia and an impaired short-term memory. She had difficulty in following commands and inability to perform calculations. Cranial nerve examination was within normal limits. Motor and sensory examinations were unremarkable except for slight tremor and decreased fine movements of the right hand. Tendon reflexes were 3+ symmetrically, with bilateral extensor plantar reflexes. Snout and sucking reflexes were elicited.

Computerized tomography (CT) revealed a homogeneous high-attenuation mass, 5 cm in diameter, filling and distorting the atrium of the left lateral ventricle (Fig. 1). The lesion appeared subjacent to the elevated choroid plexus. The left temporal and parietal lobes abutting the mass were edematous, with a slight midline shift to the right. The right lateral, third, and fourth ventricles were unremarkable. There was mild cerebral atrophy involving the right frontal and temporal cortex.

Operation. A left temporal craniotomy was performed, with the presumptive diagnosis being intraventricular meningioma. Through a middle temporal gyrus approach, a reddish-tan well-demarcated tumor was identified and judged to be entirely intraventricular. The anteromedial aspect of the mass was adherent to the choroid plexus. By alternating internal decompression of the tumor and dissection of the apparent capsule from surrounding tissues, a gross total removal of tumor was accomplished.
FIG. 1. Computerized tomography scan with contrast enhancement showing a homogeneous 5-cm mass filling the atrium of the left lateral ventricle.

**Postoperative Course.** The patient did well postoperatively, with improvement in her confusion and speech dysfunction. A subsequent abdominal CT scan and a bone scan were both negative. A CT scan of the head 2 months after the operation showed no evidence of residual tumor, and clinical evaluation at 6 months revealed no recurrence of symptoms.

**Pathological Findings.** Small fragments of rubbery to firm, red-tan tissue, \(5 \times 4 \times 4\) cm in aggregate were sent for pathological evaluation. A representative portion was frozen for immunohistochemical analysis, and another portion placed in Karnovsky II fixative for electron microscopy. The remainder was processed in 10% formalin, embedded in paraffin, and stained with hematoxylin and eosin. Immunoperoxidase studies using the avidin-biotin complex method were performed both on formalin-fixed paraffin-embedded tissue and on frozen tissue. Tissue for ultrastructural analysis was buffered in sodium cacodylate solution, dehydrated in graded ethanol, postfixed in osmium tetroxide, stained en bloc with uranyl acetate, and embedded in propylene oxide-Epon. Sections were cut 1 \(\mu\) thick and examined for representative areas of neoplasm. Ultra-thin sections were made, stained with lead citrate, and examined on a Philips 301 electron microscope.

By light microscopy, the tumor was densely cellular and was composed of wide intersecting fascicles of plump spindle cells (Fig. 2 left). The cells had long round-ended (cigar-shaped) nuclei and moderate amounts of eosinophilic cytoplasm without distinct cell borders (Fig. 2 right). Mitotic figures were frequent, but no necrosis was present. Focally, the tumor invaded the stroma of the choroid plexus.

Immunoperoxidase studies on frozen tissue demonstrated positive staining for vimentin, smooth muscle-specific actin, and desmin. The frozen tumor cells failed to stain for keratins, S-100 protein, neurofilament protein, or glial fibrillary acidic protein (GFAP). The for-
Primary intracranial leiomyosarcoma

malin-fixed paraffin-embedded tissue showed positive staining for vimentin, desmin, actin, and neuron-specific enolase, and no staining for keratins, epithelial membrane antigen, S-100 protein, or GFAP.

By electron microscopy, the tumor cells were elongated and had round-ended nuclei with occasional nuclear accordion-like contraction indentations (Fig. 3). Intracytoplasmic thin filaments were numerous, and dense bodies (dense aggregates of filaments), sometimes subsarcolemmal in location, were present. Small junctions were noted, and pinocytotic activity was focally prominent (Fig. 3 inset). The intervening stroma was of type I collagen, with focal basal lamina formation along the cellular surfaces.

Review of the slides from the mastectomy specimen showed a typical intraductal breast carcinoma without an infiltrating ductal component. All axillary lymph nodes were free of tumor. Sections of the basal-cell carcinoma were also reviewed and the diagnosis was confirmed. Neither specimen resembled the recent CNS tumor.

Discussion

Mesenchymal tumors of the CNS are uncommon. Malignant mesenchymal tumors showing myogenic differentiation are rarer still. In a review by Pasquier, et al. of primary myomatous tumors of the CNS, only one of 29 reported cases showed smooth-muscle differentiation, the remainder being pure mesenchymal or mixed neural and mesenchymal tumors showing skeletal muscle differentiation. Consequently, smooth-muscle tumors of the CNS are exceedingly uncommon, and only sporadic reports have documented primary intracranial leiomyomas and leiomyosarcomas, medulloblastomas with smooth-muscle differentiation, and metastatic leiomyosarcomas.

Most leiomyosarcomas reported in the cranial cavity have been metastatic tumors. In a review of metastatic sarcoma to the brain, Lewis found six of the 50 metastatic sarcomas to be leiomyosarcomas. Only fibrosarcoma and alveolar soft-part sarcoma were cited more frequently. Two of the leiomyosarcomas initially presented as brain lesions. Other cases have appeared, and there is the suggestion that the increasing number of reports reflects a higher incidence brought about by longer patient survival and the use of certain antineoplastic agents.

Two benign intracranial leiomyomas have been noted, occurring in the sellar and suprasellar regions. The rich vasculature of the hypophyseal-pituitary axis was proposed as a possible site of origin for these smooth-muscle tumors.

Three reports of smooth-muscle differentiation in medulloblastoma have appeared. In two cases, documented by light microscopic techniques only, there was a distinct difference between areas of spindle-shaped smooth-muscle cells and areas of typical medulloblastoma. In the third case, reported by Zülch, the atypical smooth-muscle element was believed to arise from blood vessels within the medulloblastoma. In the third report, Vuia and Hager documented, both by light and electron microscopy, a primitive neuroectodermal tumor of the posterior fossa in a 4-year-old child, which manifested both neuroblastic and smooth-muscle differentiation. Again, the suggestion was made that the smooth-muscle cells were vascular in origin.

A leiomyosarcoma believed to be primary in the dura was reported by Asai, et al. This tumor presented in a 79-year-old man as a right temporal mass which apparently arose from the dura, invaded the skull, and formed an encapsulated mass in the scalp. The authors suggested that the tumor arose from the smooth muscle in the dural vasculature.

Only one primary cerebral leiomyosarcoma has, to our knowledge, been described previously. The tumor was a sellar neoplasm in a 35-year-old man, and ultrastructural studies confirmed the smooth-muscle nature of the tumor. After subtotal resection of the tumor and postoperative radiation therapy, the patient was alive 2 years and 8 months after surgery.

As far as we can determine, the present case represents the second reported example of primary cerebral leiomyosarcoma. The pathological features are typical of smooth-muscle sarcomas in other parts of the body: cellular fascicles of spindle cells with blunt-ended nu-
nuclei, positive immunoperoxidase staining for muscle-specific actin and desmin, and electron microscopic evidence of nuclear contractions, thin filaments with "dense bodies," pinocytosis, and focal basal lamina. Review of the patient's past surgical specimens revealed tumors completely dissimilar to the current neoplasm, and clinical and radiological follow-up examinations have failed to reveal a primary malignant smooth-muscle tumor in another location.

Other mesenchymal tumors have been described as occurring in the ventricles. Scott, et al.,16 have reported a myxochondrosarcoma occurring in the fourth ventricle of a 39-year-old man, and Leedham11 described a primary rhabdomyosarcoma in a 45-year-old woman which was found to be largely intraventricular at postmortem examination.

Two possible hypotheses arise to explain the occurrence of mesenchymal tumors in the ventricles. Perhaps, as suggested by Anderson, et al.,2 in discussing their case of primary intracranial leiomyosarcoma, the tumor arose from the smooth muscle of the vasculature, akin perhaps to vascular leiomyosarcomas in other areas of the body. The rich vasculature of the choroid plexus may have provided the site of origin, just as the hypothalamic-hypophyseal vessels were proposed as the site of origin for the sellar leiomyomas discussed above. Such a hypothesis, however, would not explain the finding of tumors of skeletal muscle or cartilage in the ventricles.11,16 While skeletal muscle has been reported intracranially,18 it has not to our knowledge been noted in the ventricles. Alternatively, it has been suggested that certain sarcomas, such as rhabdomyosarcomas, arise not from dedifferentiation of mature cells (skeletal muscle in the case of rhabdomyosarcoma) but from proliferation of mesenchymal cells which undergo skeletal muscle differentiation.4 In the case of leiomyosarcoma then, one could perhaps invoke the role of a pluripotential mesenchymal cell which shows differentiation along smooth-muscle lines. Such cells could be vascular in origin, but might be components of the choroid plexus stroma16 or tela choroidea,15 or might be intraventricular meningeal17.

The present case is of clinical and radiological interest because of its unusual presentation as an intraventricular mass mimicking an intraventricular meningioma. Haykal, et al.,7 noted the radiographic similarity between meningiomas and their cases of metastatic leiomyosarcoma. The operative approach through the middle temporal gyrus to large tumors in the atrium of the lateral ventricle in either cerebral hemisphere has been associated with low morbidity. Along with the case of Scott, et al.,16 this case suggests the consideration of diverse tumors of mesenchymal origin in the differential diagnosis of intraventricular tumors.

References

18. Thieruf P, Weiland H: Über ein intrakranielles Leio-


Manuscript received November 9, 1988.