Primary Intracranial Leiomyosarcoma in an Immunocompetent Adult

Case Report

A 58-year-old man with a prior history of coronary artery disease, hypertension, and radical prostatectomy for adenocarcinoma 6 years earlier presented with a 1-week history of headache and nausea, followed by a witnessed generalized tonic-clonic seizure. The history was positive for a 100 pack-year smoking history and an absence of intravenous drug use or sexual promiscuity. The physical examination, after resolution of the postictal state, was remarkable only for a tongue bite. Routine laboratory studies and toxicology screening were normal. An initial noncontrast computed tomography (CT) scan of the brain showed a questionable tiny arachnoid cyst adjacent to the right tentorium and ethmoid sinusitis (Fig 1). A magnetic resonance imaging (MRI) scan with contrast revealed a hypodense area with loss of gray-white differentiation on T1 imaging. Postgadolinium scan showed an enhanced 1.6 × 1.4 cm mass in the left anteromedial temporal lobe (Figs 2A to 2C, arrows). There was also increased signal on T2 and flair images in the surrounding white matter suggestive of temporal lobe (Figs 2A to 2C, arrows). There was also increased signal on T2 and flair images in the surrounding white matter suggestive of edema/mass effect (Figs 2D and 2E, arrows). There was a 0.65-cm area on T2 and flair images in the surrounding white matter suggestive of temporal lobe (Figs 2A to 2C, arrows). There was also increased signal on T2 and flair images in the surrounding white matter suggestive of edema/mass effect (Figs 2D and 2E, arrows). There was a 0.65-cm area of increased signal on T2 and hypointense flair without enhancement on the postgadolinium measures in the right temporal region, likely representing a subarachnoid cyst. The differential included metastasis, primary lymphoma, meningioma, and toxoplasmosis. A CSF analysis showed a WBC count of 59 cells/µL (range, 0-5 cells/µL; lymphocytes, 42 cells/µL), glucose of 19 mg/dL (serum, 103 mg/dL), and protein of 274 mg/dL (range, 15-45 mg/dL). The Gram stain, acid-fast Bacillus smear, and cytology were negative. Serologies for Toxoplasma, fungi, Epstein-Barr virus (EBV), HIV, herpes simplex virus, and Borrelia were negative. A tumor marker panel including prostate-specific antigen (PSA) was normal. CD4 count was 599/µL (range, 359 to 1,519/µL). Whole-body CT, positron emission tomography, and bone scans were negative. A testicular ultrasound showed a small right hydrocele. While awaiting a brain biopsy after cessation of antplatelet therapy, the patient developed worsening headaches and new confusion and was readmitted within 2 weeks of initial discharge. A repeat MRI showed a mild enlargement of the left anteromedial temporal lesion at 1.6 × 1.4 cm with a new 1-cm enhancing lesion in the region of the left insular cortex (Fig 2F, arrow). Because of the location of the tumor, stereotactic biopsy was not possible, and the patient underwent a craniotomy with microdissection technique of the left temporal mass (Fig 2G, arrow indicates postsurgical margins with some postoperation hemorrhage with intraventricular extension). The dura was opened, and inspection of the area of the sylvian fissure could not identify any tumor. A clearly identifiable tumor in the anteromedial aspect of the temporal lobe was noted. Using the operating microscope and microdissection, resection of the anterior 5 cm of the temporal lobe was performed. The pathologic evaluation in the operating room showed a high suspicion for malignancy, leading to gross microsurgical resection of the tumor. Histology showed a malignant spindle cell tumor, consistent with leiomyosarcoma (Fig 3A). Immunohistochemistry revealed tumor cells focally positive for smooth muscle antigen, desmin, keratin AE1/AE3, CK7, CAM 5.2, diffusely myosin stain positive, and positive for vimentin and calponin. Tumor cells were negative for epithelial membrane antigen, CD34, S100, MART-1, CK20, TTF-1, PSA, CDX-2, CD45, GFAP, and C-KIT (CD117; Figs 3B and 3C). A Ki-67 staining demonstrated a proliferation rate of approximately 30%. Postsurgical complications included acute bilateral cerebellar infarcts, acute left middle cerebellar artery distribution infarct, associated mass effect, mild midline shift, and left uncal herniation with nodular enhancement in the region of the insula related to the residual tumor. The patient’s clinical course was further complicated by pneumonia. He died 3 weeks after the craniotomy.

Discussion

Soft tissue sarcomas constitute only 1% to 2% of all neoplasms in adults and are a highly diverse group.1,2 Of these, only 0.1% to 0.7% are in the CNS, with an estimated incidence rate of three per 10 million person-years.2-4 In previously reported primary CNS leiomyosarcomas, the age at presentation has ranged from 4 to 72 years.3,5,6 There seems to be no sex predilection, and the median duration of symptoms before presentation is approximately 4 months. The presenting features were determined by the location of the tumor. Sites of involvement have included the sellar and parasellar regions, as well as the...
pineal gland, lateral ventricle, and brainstem (both intra- and extradurally). Most CNS sarcomas represent metastases. In adults, intracranial leiomyosarcomas usually occur as a result of metastatic spread from primary sites such as the GI tract, uterus, and subcutaneous tissue. Metastatic sarcoma to the brain is also a relatively rare phenomenon, and primary intracranial sarcomas are extremely rare. Primary intracranial smooth muscle tumors can arise from the leptomeningeal linings usually with dural attachment. Pluripotent mesenchymal stem cells in the dura are probably the cells of origin. Some investigators have reported that the hemangiopericytes of intracranial blood vessels are of smooth muscle cell origin; thus, it is possible that intracerebral sarcomas may arise from the cerebral blood vessel epithelium. This may be the case for the present patient because no signs of dural origin were noted during surgery or histopathologic evaluation.

On MRI, these tumors mimic meningioma, astrocytoma, fibrous histiocytoma, primary lymphoma, and other nonmalignant lesions, such as toxoplasmosis and abscess. An association has been shown between intracranial leiomyosarcoma and EBV infection in patients with HIV and organ transplantations. An association
with previous exposure to radiation, especially in young patients, has also been reported. There are case reports of intracranial leiomyoma and leiomyosarcoma in patients, including children, who are exposed to prior radiation treatment for other conditions.\textsuperscript{17-20} Our patient’s HIV and EBV serologies were negative with a normal CD4 count, and he did not have any prior radiation exposure. In situ hybridization of the tumor specimens for EBV-encoded RNA was negative.

Significantly, our patient had a history of radical prostatectomy for a biopsy-proven adenocarcinoma of the prostate 6 years earlier, with a Gleason score of 7 (3 + 4) with approximately 40% involvement of the right lobe and 90% involvement of the left lobe and no lymphatic, vascular, or seminal vesicle invasion. On presentation, our patient’s PSA was 0 ng/mL (range, 0–4 ng/mL), with no masses noted on the whole-body CT, positron emission tomography, bone scan, or testicular ultrasound. To our knowledge, this is the first reported case of a metachronous presentation of an adenocarcinoma of prostate and an intracranial primary leiomyosarcoma.

A literature search revealed only seven case reports of primary intracranial leiomyosarcoma in adults without any association with EBV, HIV, or prior radiation exposure (Table 1). The diagnosis of leiomyosarcoma is confirmed by ultrastructural features of the smooth muscle cells and immunohistochemistry. In the present patient, the histology was consistent with leiomyosarcoma, and immunohistochemistry was positive for myosin, SMA, and desmin and negative for S100 and epithelial membrane antigen. Within the limits of radiologic and immunohistochemical analysis, the diagnosis in our patient was consistent with a primary intracranial leiomyosarcoma without dural involvement.

Leiomyosarcomas are the most malignant of all of the soft tissue tumors in terms of metastasis and poor survival rates.\textsuperscript{26,27} The prognosis of primary intracranial leiomyosarcoma has been universally poor, with the longest reported survival in the literature being 32 months.\textsuperscript{5,28} Patient survival is probably limited by the difficulty in obtaining adequate surgical margins and an adequate radiation therapy dose to the intracranial location. Intracranial and meningeal tumor spread may also limit the benefits of systemic adjuvant chemotherapy. It is difficult to predict the prognosis for intracranial leiomyosarcomas, because the treatment has not been uniform and clinical outcomes vary in the small number of reported patients (Table 1). Despite these limitations, the mainstay of treatment should probably include aggressive application of multimodality therapy.\textsuperscript{6}

The case of our patient suggests that intracranial leiomyosarcomas can be seen in immunocompetent populations. Although extremely rare, clinicians should include leiomyosarcoma in the differential diagnosis of intracranial lesions. More research is needed to understand the pathophysiology, genetics, and molecular basis of these uncommon neoplasms and to develop better predictors for prognosis, biologic behavior, and treatment.

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\textbf{AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST}

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Table 1. Reports of Adult Patients With Primary Intracranial Leiomyosarcoma

<table>
<thead>
<tr>
<th>Report of Patient Case</th>
<th>Year of Publication</th>
<th>Patient Age (years)</th>
<th>Patient Sex</th>
<th>Presenting Complaint</th>
<th>Location of the Leiomyosarcoma</th>
<th>Dural Involvement</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson et al21†††</td>
<td>1980</td>
<td>35</td>
<td>M</td>
<td>Visual symptoms</td>
<td>Sella</td>
<td>No</td>
<td>Subtotal resection and radiation</td>
<td>Alive after 2 years and 8 months†</td>
</tr>
<tr>
<td>Li et al22†‡</td>
<td>1987</td>
<td>47</td>
<td>M</td>
<td>Diplopia, ataxia, headache</td>
<td>Pineal gland</td>
<td>No</td>
<td>Subtotal resection</td>
<td>Dead at 1 year after diagnosis</td>
</tr>
<tr>
<td>Asai et al23††</td>
<td>1988</td>
<td>73</td>
<td>M</td>
<td>Rapid growth of mass</td>
<td>Right temporal mass</td>
<td>Yes</td>
<td>Resection and local radiation (60 Gy)</td>
<td>NA</td>
</tr>
<tr>
<td>Louis et al24††</td>
<td>1989</td>
<td>72</td>
<td>F</td>
<td>AMS, headache</td>
<td>Left lateral ventricle and choroid plexus</td>
<td>No</td>
<td>Gross resection</td>
<td>NA</td>
</tr>
<tr>
<td>Skullerud et al25†††‡</td>
<td>1995</td>
<td>33</td>
<td>M</td>
<td>Diplopia, headache</td>
<td>Pineal area</td>
<td>No</td>
<td>Gross microresection and radiation (54 Gy)</td>
<td>Alive after 2 years‡</td>
</tr>
<tr>
<td>Oliveira et al26††‡</td>
<td>2002</td>
<td>58</td>
<td>F</td>
<td>NA</td>
<td>Left temporal</td>
<td>NA</td>
<td>Marginal excision and radiation</td>
<td>Alive after 2.5 years‡</td>
</tr>
<tr>
<td>Hussain et al27†</td>
<td>2006</td>
<td>28</td>
<td>M</td>
<td>Parieto-occipital mass</td>
<td>Right parieto-occipital region</td>
<td>Yes</td>
<td>Gross microresection and radiation</td>
<td>Alive after 7 months‡</td>
</tr>
</tbody>
</table>

Abbreviations: M, male; NA, not available; F, female; AMS, altered mental status.

*Extensive work-up for the primary tumor or metastasis was not performed.
†Case report on immunocompetent patient, but no data on Epstein-Barr virus status are available.
‡The outcome as disclosed in the article.
§Leiomyosarcoma was part of a teratoma.
∥Epstein-Barr virus serology was negative.

REFERENCES


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