Primary Intracranial Leiomyoma in Immunocompetent Patients: Case Report, Review of Literature and Treatment Recommendations

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Abstract

Objective: Primary intracranial leiomyomas are rare tumors. These tumors are mostly described in immunocompromised patients and associated with Epstein-Barr virus (EBV). The following report is an intracranial leiomyoma that was resected twice from a young, immunocompetent male.

Methods: This is a report of a patient who initially presented with tremor and headaches. He was ultimately found to have a large 6 cm×8 cm tumor that was removed. Nine years later, he was found to have a small recurrence that was removed. No adjuvant therapies have been given.

Results: His follow-up totals well over 11 years and he remains on observation. Extensive review of this rare entity is provided.

Conclusion: It is suggested that observation without any adjuvant therapy be the treatment of choice after resection of primary intracranial leiomyomas. These uncommon, benign tumors should be followed long-term given their slow-growing nature.

Keywords: Immunocompetent; Intracranial leiomyoma; Intracranial tumors; Smooth muscle cell tumor

Introduction

Leiomyomas, benign neoplasms of mesenchymal origin, are quite common in places such as the gastrointestinal and genitourinary tracts. They are comprised of well-differentiated smooth muscle cells with few mitotic figures [1]. By convention, leiomyomas should not exhibit metastatic potential, though there have been several reported cases of metastatic leiomyomas to the lungs, heart, lymph nodes, intrapertitoneal cavity, soft tissue and muscle, breast, peripheral nerves, spinal cord and skull base [2-4]. Primary intracranial lesions remain rare. Only 17 such cases have been reported and of those, only 3 are in confirmed immunocompetent patients (Table 1) [1,5-18]. The following case is that of a 20 year-old immunocompetent male who underwent two resections of his primary, middle intracranial fossa leiomyoma with 135-month follow-up.

Case Report

History

A 20 year-old right handed Caucasian male presented in October 2001 with right-sided arm and lip tremor, weight loss, and headaches. Imaging showed a 6 cm×8 cm tumor originating in the left middle fossa (Figures 1A and B). Surgical removal was recommended at this time and a combined neurosurgery/neuro-otology approach was performed. The tumor was quite vascular. It was noted at the time of surgery that the tumor invaded the temporal bone into the soft tissues and also involved the dura. Following gross total resection, the tumor was found to be a well-differentiated, Epstein-Barr virus (EBV) negative, primary intracranial smooth muscle tumor. A subsequent complete workup revealed no other sites of disease. No adjuvant therapy was recommended secondary to achieving gross total resection (Figures 1C and 1D). Postoperatively, the patient developed a slight expressive aphasia and a partial right homonymous hemianopia; both had complete resolution. Nine months postoperatively, the patient presented with seizures and was started on lamotrigine with adequate control. Over the following four years, the patient had routine follow-up imaging that did not show any recurrence of the tumor. The patient was then lost to neurosurgical follow-up and had remained asymptomatic and seizure-free off lamotrigine until 2010. At this time, a CT scan was obtained to evaluate hearing loss. A small encephalcele from the prior operation was thought to be contributing to a conductive hearing loss. An MRI was performed that showed an 8 mm tumor recurrence in the floor of

Figure 1: (A and B) Axial and coronal, pre-operative, post-contrast T1 MRI of middle fossa tumor. (C and D) Axial and coronal post-contrast T1 MRI showing gross total resection.
A joint operation with neuro-otology and neurosurgery was performed in order to address both issues of hearing loss and tumor.

### Patient Information

| Patient | Author | Year | Age (years) | Sex | Size (cm) | Location | Immune Status | EBV Status | Pathological features | Surgery | Adjuvant therapy | Follow-up (months) | Status |
|---------|--------|------|-------------|-----|-----------|----------|---------------|------------|------------------------|---------|------------------|------------------|--------|
| Adult   | Hua et al. [1] | 35M | 3.0 | R middle fossa; extradural | HIV | (+): SMA, vimentin (-): S100, EMA, CD34, MIB-1 | GTR | None | 18 | NR | |
| Immunocompromised | Adult | Kleinschmidt-DeMasters et al. [11], Case 4 | 34F | 1.2 | R cavernous sinus; intradural | HIV | (+): MSA, desmin, EBV RNA | STR | None | 4.5 | |
| Immunocompromised | Adult | Karpinski et al. [9] | 26M | 3.0 | 1. L sphenoid ridge; intradural 2. C2/C3 lesion; intradural, extramedullary | HIV | (+): actin, EBV (-): EMA, S100 | STR | None | -- | |
| Immunocompromised | Adult | Bargiela et al. [6] | 32F | 5.0 | L occipital lobe; intradural | HIV | -- | (+): MSA, desmin, low mitotic activity | Autopsy | -- | -- |
| Pediatric | Kumar et al. [13] | 10M | 4.0 | R basal ganglia; intradural | HIV | (+): MSA, desmin, EBV, rare mitoses (-): S100 | GTR | None | 6 | NR | |
| Pediatric | Unpublished | 8F | 0.8 | 1. frontal; intradural 2. sylvian fissure; intradural | HIV | ND | (+): low MIB-1 (-): p53, EBV ND | STR | None | -- | |
| Immune status unknown | Adult | Bette et al. [11] | 56F | 3.2 | sellar/suprasellar; intradural | -- | (-): MSA, vimentin, S100 in cytoplasm (-): myoglobin, desmin, ER, PR, GFAP, EMA, pancytokeratin, EBV | GTR | None | 6 | NR | |
| Immunocompromised | Adult | Ali et al. [5] | 29F | 1.2 | R frontal floor; intradural | -- | (-): MSA, MSA, Collagen IV desmin, caldesmon, Ki-67<1% (-): keratin, EMA, S100, CD117, ER, PR, CD34, CD30, EBV | GTR | None | -- | |
| Immunocompromised | Adult | Kim et al. [10] | 40F | 7.0 | R temporal parietal; intradural | -- | (+): vimentin, SMA | GTR | None | -- | |
| Pediatric | Caucasian | 68F | 3.0 | sellar; intradural | -- | Diagnosis was based solely on histologic appearance | STR | None | 9 | NR | |
| Immunocompromised | Adult | Kazumoto and Matzumoto [18] | 38F | 3.5 | R temporal lobe; intradural | -- | (+): SMA, vimentin, desmin (-): GFAP, human factor 8 related antigen | GTR | None | 10 | NR | |
| Immunocompromised | Adult | Lin et al. [14] | 20F | 3.0 | L temporal and insular; intradural | -- | (+): vimentin, muscle actin, desmin (-): S100, neurofilament, GFAP, EMA, ER, cytokeratin | Bx | None | 10 | NR | |
| Pediatric | Pediatric | 4F | 5.0 | suprasellar; intradural | -- | Diagnosis was based solely on histologic appearance | STR | None | -- | |
| Pediatric | Pediatric | 12M | -- | R temporal; intradural | -- | (+): SMA (-): S100, GFAP, vimentin, desmin, neuron specific enolase | GTR | None | 56 | NR | |

### Table 1:

**Note:**

- **=status post solid organ transplant and subsequent immunosuppressive therapy.**
- **Bx=Biopsy; CK=Cytokeratin; EMA=Epithelial Membrane Antigen; ER=Estrogen Receptor; GFAP=Gliarial Fibrillary Acidic Protein; GTR=Gross Total Resection; L=Left; MIB-1=Monoclonal Antibody against Ki-67 antigen; MSA=Myosin-Specific Actin; ND=Non-Diagnostic; NR=No Recurrence; PR=Progesterone Receptor; Prog=Progression; R=Right; Rec=Recurrence; S100=Smooth Muscle Actin; STR=Subtotal Resection;

- **Middle fossa (Figures 2A and 2B). In addition, there was a separate 1.5 cm lesion in the left frontal bone which was also appreciated on clinical examination (Figures 2C and 2D). The patient sought a neurosurgical opinion in regards to the recurrent tumor.**

**Operation**

A joint operation with neuro-otology and neurosurgery was performed in order to address both issues of hearing loss and tumor...
Primary intracranial leiomyomas are a rare entity and even rarer in an immunocompetent patient. The majority of intracranial leiomyomas are discovered in immunocompromised patients [3,5,7,9,11,17]. Their immunosuppression stems from HIV infection, pharmacologic suppression after organ transplantation, or genetic disorders such as common variable immunodeficiency syndrome. Many of the lesions in this patient population are positive for EBV [3,5,7,9,11,17]. In our patient, however, the immune system was intact and the lesion was negative for EBV, making a total of 4 cases in the immunocompetent patient reported in the literature [1,5,8,11].

Though there seems to be predilection for immunocompromised patients, intracranial leiomyomas affect both sexes equally, most commonly in the second and third decades of life [1]. The majority of patients do not present with symptoms, however, and the lesions are often found incidentally [1]. Imaging can aid in suggesting the diagnosis of an intracranial leiomyoma due to its characteristic features. On MRI, leiomyomas will appear as a homogenous iso- or hypointense lesion on T1-weighted imaging and as a heterogeneous hyper- or hypointense lesion on T2-weighted imaging; hypointensity is reported most commonly [1,5-8,16,19]. They enhance with contrast administration and their appearance is most similar to meningioma.

Though the imaging can aid in narrowing the differential diagnosis, immunohistochemistry must be done in order to confirm the diagnosis. Upon staining, a leiomyoma will be positive for alpha-actin, desmin, myosin, and vimentin, and negative for S100 [1,20,21]. Histology reveals spindle shaped cells with blunt ends and few mitotic figures, which help in distinguishing it from the highly malignant leiomyosarcoma with a high number of mitotic figures and strong expression of MIB-1 [1,22].

The best treatment option to date for primary intracranial leiomyomas remains surgical gross total resection without adjuvant radiation therapy [1]. There is one case report in the literature that postulates an intracranial leiomyoma transitioning to leiomyosarcoma post radiation therapy therefore suggesting that if a resection is subtotal, observation may be warranted [23]. No general recommendations for long-term follow-up have been made secondary to the paucity of data, rarity of the disease, and the trend that the majority of the patients suffers from the disease.

**Second operation:** The recurrent tumors from the left frontal bone and left middle temporal fossa were morphologically similar. Both appeared more differentiated than the original tumor, as evidenced by abundant eosinophilic cytoplasm and the formation of distinct bundles of smooth muscle (Figure 3C). Only a rare mitosis was encountered, and there was no necrosis. The Ki67 immunolabeling index was 2%. The tumor cells showed strong diffuse expression of smooth muscle actin and smooth muscle myosin (Figure 3D). ISH for EBER was negative. Invasion of bone in the left frontal region was confirmed.

**Pathological findings**

**First operation:** The original tumor was a smooth muscle neoplasm composed of intersecting fascicles of spindle cells with eosinophilic cytoplasm and elongated blunt-ended nuclei with small nucleoli (Figure 3A). There was focal degenerative-type necrosis with fibrosis and dystrophic calcification. Mitoses were rare and difficult to find. The Ki67 immunolabeling index was 1.3%. Tumor cells showed strong diffuse expression of smooth muscle actin, muscle-specific actin, and desmin by immunohistochemistry (Figure 3B). In situ hybridization (ISH) for Epstein-Barr virus early RNA (EBER) was negative. Immunostains for S100 protein, EMA, GFAP, and latent membrane protein (EBV) were negative. Due to the presence of bone invasion, the malignant potential was considered uncertain.

**Postoperative course**

Postoperatively, the patient did well and remained neurologically intact. The postoperative imaging revealed gross total resection. Again, no adjuvant therapy was recommended given the slow growing nature of this tumor, the extent of resection, and the pathological findings. Five months post-resection, the patient presented with a seizure and was restarted on lamotrigine without further seizure activity. The patient continues to be recurrence-free 24 months after the second resection, for a total survival length of 135 months from the initial diagnosis in 2001. Surveillance imaging was every six months, consisting of MRI with and without contrast to assess for tumor recurrence. This was recently extended to one year intervals.

**Discussion**
with primary intracranial leiomyomas are immunosuppressed and have therefore died from other co-morbidities [3,5-7, 9,11,17]. Our patient had a small recurrence found 108 months after his primary resection. Table 1 identifies similar intracranial cases with the longest follow-up of 84 months [17]. These cases illustrate the need for long-term follow-up in patients with this rare disease given both its slow-growing nature and prolonged recurrence time frame. In addition, it is suggested that resection be followed by observation only considering the protracted course of these tumors in both the immunocompetent and immunocompromised patient.

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