Pituitary aspergillosis presenting as a sellar mass with compressive symptoms in an immunocompetent patient.

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Abstract

Objectives:

Pituitary aspergillosis is a very rare condition with only 18 cases reported. Nonetheless, it should be included in the differential diagnosis for a sellar/parasellar mass as early recognition is key to successful management. We present a case report and review of the literature.

Case Report:

A 67-year-old woman presented with months of headache and worsening vision, found to have unilateral temporal hemianopsia and abducens palsy. Initial MRI was unremarkable, but later imaging showed a large sellar/suprasellar mass encroaching into the right cavernous sinus and abutting the optic chiasm. Preoperative pituitary endocrine panel was normal and there was no history of paranasal sinus disease. She was diagnosed with a pituitary macroadenoma.

Results:

The patient underwent resection of the mass via endoscopic trans-sphenoidal approach. Intraoperatively it was noted to be soft and tan-pink with multiple fibrous septations. Initial pathology showed hypophysitis with mixed inflammation and focal necrosis. She had an uncomplicated immediate postoperative course. Pathology review including Gomori methenamine-silver stain showed hyphae consistent with Aspergillus. PCR testing also detected Aspergillus fumigatus DNA. She was readmitted on postoperative day twelve with weakness, gait instability, and headache, at which point she was treated for adrenal insufficiency. IV amphotericin B was administered followed by oral voriconazole. Ten weeks post-operatively her headache has resolved, vision remains stable, and she shows no evidence of active infection.

Conclusion:

Sellar aspergillosis should be considered in the differential diagnosis of a sellar mass, as it is difficult to diagnose preoperatively and may present similarly to a pituitary neoplasm or apoplexy in an immunocompetent patient. It can be successfully treated with prompt surgical extirpation and systemic antifungals.

Case Report

A 67-year-old woman initially presented to her primary care physician with persistent headache. An MRI at that time showed no overt pathology and her symptoms were treated with analgesics. Three months later she began experiencing diplopia and blurry vision in her right eye. Initial exam indicated binocular horizontal diplopia, and right orbit esotropia in primary gaze. Visual acuity was normal. A second MRI showed a pituitary mass measuring 2.4 cm, which was presumed to be a pituitary macroadenoma. In the two weeks before her scheduled neurosurgery appointment, her visual symptoms quickly progressed and she presented to the emergency department. There she was found to have loss of light perception from the right eye and complete abducens nerve palsy, and was diagnosed with pituitary apoplexy secondary to an enlarging adenoma. She denied symptoms aside from her headache and changes in vision. She was immediately scheduled for surgery due to the rapid progression of visual deficits. Preoperative testing showed no abnormalities of pituitary endocrine function. The immediate preoperative MRI is shown in Figure 1.

An endoscopic trans-sphenoidal technique was used to approach the mass, which was found protruding down through the eroded floor of the sella. Some residual extensions toward the right optic canal and cavernous sinus remained after the surgery and a small cerebrospinal fluid leak was repaired with a primary dural repair.

The mass was composed of tan-pink soft tissue and noted to contain multiple fibrous septations. It was not inconsistent with macroadenoma, which can have varied appearances upon gross examination.

Preoperative MRI

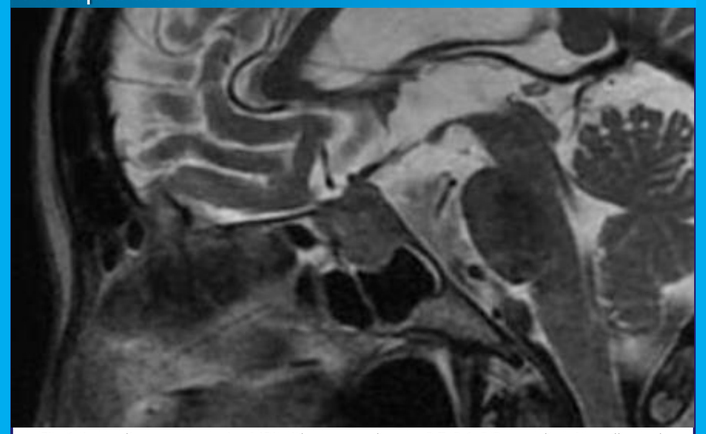

Fig. 1. Immediate pre-operative MRI with contrast shows a 2.7x2.1x2.0 cm enhancing sellar and suprasellar mass with internal cystic components. There is upward impingement on the optic chiasm, worse on the right, and the right cavernous carotid was encased by the lesion and slightly narrowed. The mass also abutted the medial aspect of the left cavernous carotid artery. The Circle of Willis was complete.

Case Report (continued)

Upon histological examination, the specimen was found to be consistent with hypophysitis, without features suggestive of adenoma. Grocott's modified methenamine-silver stain (GMS) was performed a few days later and showed septated hyphae consistent with Aspergillus spp. A sample of the mass was sent for PCR analysis to confirm the diagnosis. Immediate postoperative MRI showed decompression of the optic chiasm, but persistent encasement of the right cavernous sinus and narrowing of the right carotid artery. The patient's steroid regimen was stopped on post-operative day nine due to concern for immunosuppression, with instructions to present to the emergency room if she experienced any symptoms of adrenal insufficiency or panhypopituitarism. Twelve days post-operatively and three days after stopping the steroid regimen, the patient presented to the ED with weakness and instability due to secondary adrenal insufficiency. She was started on steroids and IV amphotericin B, and was transitioned to oral voriconazole when Aspergillus was identified in the tissue by GMS and confirmed by PCR. The patient was stabilized and discharged on oral voriconazole and cortisol replacement for the next six months, during which time she showed no signs of active infection. Her headache is resolved, but her right-sided vision loss and abducens nerve palsy remain. Post-operative imaging at three and six months showed stable residual enhancing soft inflammatory tissue in the right cavernous sinus with extension toward the right optic canal. An MRA at six months showed a focal severe stenosis of the right internal carotid artery at the distal cavernous and proximal supraclinoid segment, but good reconstitution distally from the contralateral side. Given the difficulty of eradicating Aspergillus, the decision was made to continue voriconazole until there is more definitive evidence of resolution. Cortisol replacement has been stopped and she has no other signs of hypopituitarism.

Discussion

Review of existing case reports finds that although fungal pituitary infection is nearly always initially misdiagnosed as pituitary macroadenoma, an infectious pathology often becomes apparent during surgery as pus, debris, necrosis, and inflammation are found. Eighteen English language case reports exist. Of thirteen prior case reports that mentioned a pre-operative diagnosis, seven suspected pituitary adenoma and only two suspected an infectious etiology prior to surgery[8, 12]. Of the known cases in the literature, fourteen had intraoperative findings that led them to suspect an infectious etiology. In the case presented here, the mass contained fibrous septations rather than pus and debris, a presentation similar to a case reported by Furtado et al.[3] in which the lesion was described as "avascular and firm". In each case where a description of the histological diagnosis was available, Grocott's/Gomori methenamine-silver stain revealed hyphae consistent with Aspergillus infection.

Notably few of the reviewed cases report endocrine abnormalities. Visual deficits were prominent for twelve patients whose presenting symptoms were described, while only six cases[5-10] detailed new abnormal pituitary function. The visual deficits often present and progress quickly, as with our patient. Return to baseline vision is possible but occurred in only a few cases. Encasement of the internal carotid artery can cause severe focal stenosis, and early treatment is important to avoid carotid artery narrowing bilaterally. Our patient has a complete Circle of Willis allowing good collateral flow.

Many cases have a delayed confirmation of etiology due to the expectation of a tumor rather than fungus. This is likely why many patients begin therapy with amphotericin B or caspofungin before switching to an oral medication. Treatment with oral voriconazole is considered appropriate, although two cases[1,2] showed long-term resolution without systemic therapy. Given the high mortality of intracranial fungal infections, it is best to err on the side of overtreatment. Of the reviewed cases, five patients died soon after diagnosis.

Aspergillus can reach the sella via several different pathways; by direct invasion from the paranasal sinuses, by hematogenous dissemination from another site such as the respiratory tract, or by introduction during a surgical procedure. This patient had never had surgery of the sinuses, skull base, or cranium, and while the pathology showed some signs of inflammation in the nasal mucosa, no gross changes were seen intraoperatively. There was no indication of disease in the rest of her respiratory tract. Why the Aspergillus was able to grow and invade is another question altogether. Aspergillus is ubiquitous but will usually only affect patients with compromised immune systems. Of the ten reviewed cases that reported comorbidities, six had diabetes mellitus, one with a kidney transplant, one had hemolytic anemia, and another had a history of pituitary surgery and previous radiation. Our patient had no apparent cause for immunodeficiency and the reason for her infection remains unclear.

Conclusions

Sellar aspergillosis is a rare condition, which is often misdiagnosed as an adenoma and can have a varied appearance intraoperatively. It is best diagnosed using Grocott's/Gomori methenamine- silver stain, and has a good prognosis if treated early with surgery and appropriate antifungal therapy.

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