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Acute Chiasmal Abscess Resulting from Perineural Extension of Invasive Sino-Orbital Aspergillosis in an Immunocompetent Patient

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Abstract

OBJECTIVE—Intracranially invasive sino-orbital aspergillosis is a rare entity seen predominantly in immunocompromised individuals. We report a unique case of an acute chiasmal abscess resulting from perineural extension of an indolent invasive sino-orbital aspergillosis in an immunocompetent patient.

CASE DESCRIPTION—A 61-year-old healthy Ukrainian man presented with severe left retro-orbital pain and a gradual ipsilateral monocular vision loss with rapid progression to a contralateral temporal visual field cut. He was found to have an intracranially invasive sino-orbital *Aspergillus fumigatus* infection with perineural extension along the optic nerve complicated by an acute chiasmal abscess.

RESULTS—The patient was managed with surgical debridement and adjuvant antifungal chemotherapy. The patient's life and vision were preserved.

CONCLUSIONS—The case demonstrates that it is possible to successfully control advanced intracranial aspergillosis with tissue-sparing surgery and adjuvant antifungal chemotherapy in immunocompetent individuals.

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Keywords

Chiasmal abscess; Immunocompetent patients; Invasive sino-orbital aspergillosis; Perineural extension; Vision loss

INTRODUCTION

Aspergillosis of the paranasal sinuses usually is self-contained and has a favorable prognosis. In contrast, invasive disease may result in significant morbidity from intra-orbital and intracranial extension. Invasive sino-orbital disease usually occurs in debilitated patients with diabetes mellitus, cirrhosis, human immunodeficiency virus, or leukemia; those who undergo long-term systemic corticosteroid therapy; those who are drug abusers or alcoholics; or those who are older (7, 25, 37, 44). Intracranial extension often results in mortality despite therapy. Nonetheless, invasive sino-orbital aspergillosis may occur in immunocompetent patients (3, 17, 18, 29, 30, 32, 35, 43). The standard treatment for invasive sino-orbital disease has been radical surgical intervention, including orbital exenteration, sinus excision, and aggressive intracranial debridement (9, 13, 22, 31). However, more recently, good outcomes have been reported with a combination of limited surgical debridement and antifungal drug therapy, especially in immunocompetent patients (1, 21, 27). We present a case of invasive sino-orbital aspergillosis with perineural extension along the optic nerve complicated by an acute chiasmal abscess in an immunocompetent patient. The patient was successfully managed with surgical debridement and adjuvant antifungal chemotherapy.

CASE REPORT

History and Examination

A 61-year-old healthy man, a recent refugee from the Ukraine, presented to The Johns Hopkins Hospital ophthalmology clinic with a 10-month history of progressive vision loss in the left eye and severe ipsilateral retro-orbital pain. He reported having a diagnosis of a left sinus, orbital, and intracranial mass, with history of equivocal biopsy results, previously treated by multiple intraorbital steroid injections in Ukraine for presumed inflammatory pseudotumor. His medical history included only hypertension. On review of systems, he complained of a recent 20-lb weight loss, nausea, and depression. Findings from the initial ophthalmic and neurologic examinations demonstrated light perception vision in the left eye and 20/30 vision in the right eye. The patient had marked proptosis, limitation of extraocular motility, ptosis, and a large afferent pupillary defect on the left side. Funduscopy evaluation was notable for left optic disk pallor. The rest of the findings from his physical examination were unremarkable. The patient was admitted to the neurosurgical unit, and a computed tomography scan of his head followed by a brain magnetic resonance imaging (MRI) were performed.

Neuroimaging and Hospital Course

The patient's imaging studies demonstrated an enhancing soft-tissue mass infiltrating the left optic nerve with extension towards the left aspect of the chiasm. There was an associated

expansion of the left optic canal with sclerosis of the anterior clinoid process and invasion of the adjacent sphenoid and ethmoid sinuses by the mass (Figure 1A–D). An endonasal endoscopic transtethmoidal and transorbital biopsy of the mass revealed fibrous tissue with chronic inflammation and branched hyphal fungal forms.

A thorough medical work-up, including testing for human immunodeficiency virus, did not reveal any evidence of an immunocompromised state or systemic fungal infection. Given the patient's immunocompetence and relatively indolent disease progression, he initially was managed conservatively with intravenous liposomal amphotericin B (5 mg/kg/per day). Two days after his biopsy, however, the patient noted an acute onset of a right temporal field deficit. A repeat MRI of the brain showed a new contrast-enhancing mass with a hypointense, loculated center, extending towards the right aspect of the chiasm and proximal right optic nerve (Figure 2A). Automated perimetry confirmed the visual field loss (Figure 2B). Given the clinical and radiographic progression, an emergent frontosphenotemporal craniotomy with resection of necrotic tissue infiltrating the left optic nerve and chiasm, orbit, and ethmoid sinuses was performed. Intraoperatively, a chiasmal abscess extending to the proximal right optic nerve, corresponding to the new lesion on the MRI, was found (Figure 2C). The chiasmal abscess was debrided with sparing of the right lateral aspect of the capsule to preserve the remaining vision in the right eye. Postoperatively the patient retained good visual acuity in the right eye with a stable right temporal field defect. Microscopic analysis and fungal culture of the obtained specimen were consistent with *Aspergillus fumigatus* (Figure 3A–C). Antifungal therapy with intravenous voriconazole and micafungin was administered for 2 weeks with resolution of the enhancement within the right optic nerve and chiasm. The patient was discharged on oral voriconazole (300 mg twice daily).

The patient is now 1 year out from his surgery and remains on oral voriconazole. His current imaging studies demonstrate no enhancement along the chiasm and right optic nerve (Figure 4A). His visual field has improved (Figure 4B), and his visual acuity remains stable.

DISCUSSION

Invasive sino-orbital aspergillosis is seen primarily in immunocompromised patients and often results in significant morbidity and mortality; it occurs rarely in immunocompetent patients. To our knowledge, there have only been 18 cases of sino-orbital invasive *Aspergillus fumigatus* infection in immunocompetent individuals reported in literature between 1913 and 2012 (Table 1), and more than half of these cases have been described in the past 20 years (2, 5, 6, 10, 11, 15, 16, 20–22, 24, 32, 35, 36, 38, 40–42, 45).

Making an early diagnosis of invasive sino-orbital aspergillosis in immunocompetent patients can be challenging. Similar to our patient, Sivak-Callcot et al. (35) reported a delay in diagnosis of up to 10 months as the result of nonspecific complaints of retro-orbital pain preceding the ophthalmic findings by 1–6 months. Indeed, 14 of 18 (78%) previously reported patients initially presented with persistent unilateral, severe, frontal headache, or retro-orbital pain as their chief complaint (2, 24, 32, 35). Several of these patients were diagnosed initially with temporal arteritis or orbital pseudotumor and were treated with

high-dose systemic corticosteroids (5, 6, 12, 14, 16, 36, 38, 41). Therefore, even in healthy patients, a complaint of persistent and/or escalating retro-orbital pain with or without ophthalmic findings should prompt the physician to order orbital and cranial imaging studies before making a diagnosis and initiating therapy. Because the orbital findings are often nonspecific, the clinician should have a low threshold for further work-up. Computed tomography or MRI findings of paranasal sinus and orbital mass and/or bone destruction (with or without optic nerve involvement) should be investigated by a biopsy to rule out fungal infection.

The pathophysiology of invasive aspergillosis in immunocompetent host is uncertain. It is thought that predisposing factors for both invasive and noninvasive types of infections include mechanical obstruction of the nose and paranasal sinuses, such as septal abnormalities, allergic rhinosinusitis, nasal polyps, and infections (23, 33). These risk factors, however, were not present in our patient. Intracranial spread of fungus via bone erosion and migration along the blood vessels has been reported previously (8, 23, 33), but fungal spread via perineural extension along the entire length of the optic nerve to involve the chiasm, as occurred in our patient, has not been described in an immunocompetent patient. The reason for this spread and acute disease progression in the setting of a previously indolent process remains unclear. It is possible that the initial endonasal endoscopic biopsy breached existing physical barriers with subsequent rapid spread of the infection. Perhaps, early initiation of antifungal chemotherapy based on clinical and radiographic data before biopsy, or performing a biopsy of the involved sinuses alone, without entering the orbit and the optic canal, would have been helpful in reducing the acute progression of the disease. Alternatively, upon confirmation of the diagnosis via a frozen section at the initial procedure, a more aggressive debridement could have been undertaken with concomitant initiation of antifungal chemotherapy.

Management of invasive sino-orbital Aspergillosis in immunocompetent patients remains an area of controversy. Recommendations have ranged from medical management alone to radical surgery with adjuvant chemotherapy (4, 27, 28, 35). Combination antifungal therapy with amphotericin B and itraconazole, voriconazole, or micafungin with or without surgical intervention has been used successfully to control the infection in some cases (3, 19, 26, 28, 34, 35). Voriconazole recently has become the drug of choice for invasive aspergillosis because patients demonstrate a better tolerance for it and because of its lower toxicity compared with amphotericin B (3); the overall response rate to antifungal chemotherapy ranges from 40% to 60% (39). We initially treated our patient medically because of the relatively indolent disease course. After his clinical and radiographic deterioration, an emergent aggressive debridement with adjuvant chemotherapy was required to successfully control the disease and preserve his remaining vision. Given high rates of morbidity and mortality after radical debridement of invasive fungal disease, we believe that even in a more widespread intracranial infection, a tempered approach may be reasonable in immunocompetent patients.

CONCLUSIONS

Invasive sino-orbital aspergillosis, although rare, can still present in immunocompetent patients. We described a novel route of intracranial invasion in an otherwise-healthy patient via a perineural spread along the optic nerve to involve the chiasm. Early diagnosis of this infection is critical to successful management. Nonspecific complaints or retro-orbital pain should prompt the physician to consider this diagnosis. The radiologic findings of optic nerve and/or chiasmal infiltration with associated adjacent paranasal sinus involvement should lead the clinician to consider an urgent tissue biopsy to rule out aspergillosis. If the infection is confirmed, we recommend urgent initiation of antifungal chemotherapy in conjunction with immediate surgical debridement with the goal of preserving life and structures of vital function (e.g., optic nerve, chiasm). Our case demonstrates that it is possible to successfully control advanced intracranial aspergillosis with tissue-sparing surgery and adjuvant antifungal chemotherapy in immunocompetent patients.

Abbreviations and Acronyms

MRI Magnetic resonance imaging

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Figure 1.

(A–C) T1-weighted magnetic resonance image of the brain demonstrates a contrast enhancing mass along the left optic nerve extending into the ipsilateral sphenoid sinus and towards the left aspect of the chiasm. (D) Noncontrast computed tomography of the head demonstrates hypodense material in the left ethmoid and sphenoid sinuses with bony erosion, expansion of the ipsilateral optic canal, and sclerosis of the anterior clinoid process.

Figure 2.

(A) T1-weighted magnetic resonance imaging (MRI) of the brain demonstrates a new ring-enhancing, loculated, cavitary chiasmal lesion, contiguous with the mass seen on the patient's admission MRI scan with extension towards the right aspect of the optic chiasm and proximal origin of the right optic nerve. (B) Humphrey visual field test of the right eye demonstrates the acute temporal field defect noted by the patient. (C) Intraoperative view of the edematous left optic nerve (LON), right optic nerve (RON), and internal carotid artery (ICA).

Figure 3.

Photomicrograph of the surgical specimen stained with hematoxylin and eosin (**A**) and Grocott's methenamine silver (**B**) revealing findings of septate, acute-branching aspergillus hyphae. Periodic acid-Schiff (**C**) stain shows fungal forms (*FF*), tissue necrosis (*TN*), and optic nerve fibers (*ONF*).

Figure 4. Postoperative T1-weighted magnetic resonance image of the brain demonstrates decreased enhancement of the remaining chiasm (A) corresponding to an improved right temporal visual field deficit (B).

Table 1
Review of Sino-Orbital Invasive *Aspergillus fumigatus* in Immunocompetent Individuals

Case	Age, Sex	Location	Extension *	Treatment	Outcome [†]
Dalmeijer (10)	65, F	Orbit	Lungs, brain	Orbital exenteration	Death 2.5 months later
Townes (42)	31, M	Lung	Orbit	Orbital exploration; amphotericin B	Alive at 3 weeks
Hedges and Leung (14)	62, F	Orbit	Brain	Debridement and amphotericin B; steroids	Death 5 months later
Yu et al. (45)	37, M	Sphenoid sinus, nasopharynx	Orbit, sella turcica	Sphenoidotomy; amphotericin B; rifampin	Alive at 1 year
Spoor et al. (38)	49, F	Sphenoid sinus	Orbital apex, internal carotid artery, basal ganglia, midbrain, cerebellum	Amphotericin B and rifampin; steroids	Death 2 months later
Austin et al. (5)	77, M	Orbit	Orbital apex, cavernous sinus, internal carotid, middle and anterior cerebral arteries	Orbital exenteration; amphotericin B; steroids	Death 3 months after diagnosis
Fuchs et al. (11)	48, F	Sphenoid sinus	Orbit, ethmoid sinus, sella turcica	Surgery; amphotericin B; rifampin	Alive at 1 month
Lowe and Bradley (20)	74, F	Ethmoid sinus	Orbit, frontal lobes	None	Death 12 months later
Bradley et al. (6)	74, F	Ipsilateral paranasal sinuses, orbital apex	Cavernous sinus, anterior and middle cranial middle fossa	Amphotericin B; flucytosine; ketoconazole; vibunazole; steroids	Alive at 2 years
Slavin (36)	65, M	Orbital apex	Ethmoid and sphenoid sinuses	Amphotericin B; steroids; antibiotics, acyclovir	Death 2 weeks later
Heier et al. (15) (case 3)	21, F	Paranasal sinuses	Orbit	Amphotericin B	Alive at 6 months
Mauriello et al. (22) (case case 5)	71, F	Sphenoid and ethmoid sinuses	Orbit, Dura	Debridement; amphotericin B then liposomal amphotericin B; local amphotericin B	Death 2 months later
Suzuki et al. (41)	83, F	Sphenoid and ethmoid sinus	Orbital apex, optic canal, skull base, middle cerebral artery	Steroids	Death 6 months later
Massry et al. (21)	40, F	Paranasal sinuses	Orbit	Debridement; amphotericin B; itraconazole	Alive at 2 years
Hutnik et al. (16)	75, M	Posterior ethmoid sinus, sphenoid sinus	Orbital apex, optic canal, cavernous sinus, superior orbital fissure, inferior frontal lobe, meninges	Amphotericin B and fluconazole; steroids	Death 2 months later
Streppel et al. (40)	50, F	Paranasal sinuses	Orbit, skull base	Amphotericin B; debridement; liposomal amphotericin B; postoperative itraconazole	Death 16 months later
Sivak-Callcott et al. (35) (case 2)	77, M	Sphenoid sinus	Orbital apex, pterygopalatine fossa, infraorbital fissure, anterior cavernous sinus	Amphotericin B; local amphotericin B; oral itraconazole	Alive 13 months later

Case	Age, Sex	Location	Extension *	Treatment	Outcome†
Sivak-Callcott et al. (35) (case 3)	73, F	Sphenoid sinus, orbital apex	Cavernous sinus, inferior orbital fissure, temporalis fossa, extraocular muscle	Amphotericin B; liposomal amphotericin B and rifampin; itraconazole; steroids	Death 18 months later

* Extension implies either a contiguous spread from the original lesion or a fungal metastasis to a distant organ.

† The time to final outcome is determined from the diagnosis to the last reported follow-up date.