

# Cavernous sinus-orbital apex aspergillus infection in a diabetic patient

## A case report

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### Abstract

**Rationale:** Cavernous sinus-orbital apex aspergillosis is a rare but serious complication of rhinosinusitis. Pathology results are scarce, and this condition is difficult to diagnose based on clinical and radiological results.

**Patient concerns:** A 64-year-old woman presented with cavernous sinus-orbital apex syndrome. Axial and sagittal T1 contrast-enhanced magnetic resonance imaging (MRI) showed a right orbital apex mass abutting the right posterior ethmoid sinus, sphenoid sinus, and cavernous sinus.

**Diagnosis:** Cavernous sinus and orbital apex aspergillosis.

**Interventions:** Functional endoscopic sinus surgery was performed, and a biopsy of the lesion tissue was submitted for examination, which showed the presence of aspergillus.

**Outcomes:** One year after surgical debridement, antifungal, and anticoagulation treatments, the patient is still asymptomatic without recurrence.

**Lessons:** Early surgical debridement is crucial to confirm the diagnosis of cavernous sinus-orbital apex aspergillosis and prevent mortality. There is no evidence of negative effects of antibiotic and anticoagulation treatments. Despite controversy, among physicians, most opt to treat patients via anticoagulation therapy.

**Abbreviations:** CNS = central nervous system, CSF = cerebrospinal fluid, MRI = magnetic resonance imaging.

**Keywords:** aspergillosis, cavernous sinus, orbital apex, rhinosinusitis

## 1. Introduction

Cavernous sinus and orbital apex aspergillosis is a rare and potentially fatal infection. The lack of specific clinical manifestations and deep anatomic location, increase the difficulty of an early diagnosis.<sup>[1,2]</sup> Aspergillus infections are usually divided into noninvasive and invasive infections. Invasive aspergillosis can penetrate the blood vessels and central nervous system (CNS). This

type of infection is often found in immunocompromised patients with type 2 diabetes mellitus, long-term corticosteroid use, hematologic malignancy or HIV infection.<sup>[3,4]</sup> Some case reports indicate that aspergillosis is misdiagnosed as tumor metastasis,<sup>[5,6]</sup> which delays treatment. However, aspergillus infections rarely invade both the cavernous sinus and orbital apex. In our paper, an example is described of aspergillus infection of the paranasal sinuses involving both the cavernous sinus and orbital apex of an elderly female patient. This article illustrates the clinical features, radiographic findings, pathology and treatment of such a case. Early identification of cavernous sinus and orbital apex aspergillosis is possible using pathological results when physicians are aware of this condition.<sup>[3,4,7]</sup> Early use of antifungal treatment is effective and reduces the risk of mortality.

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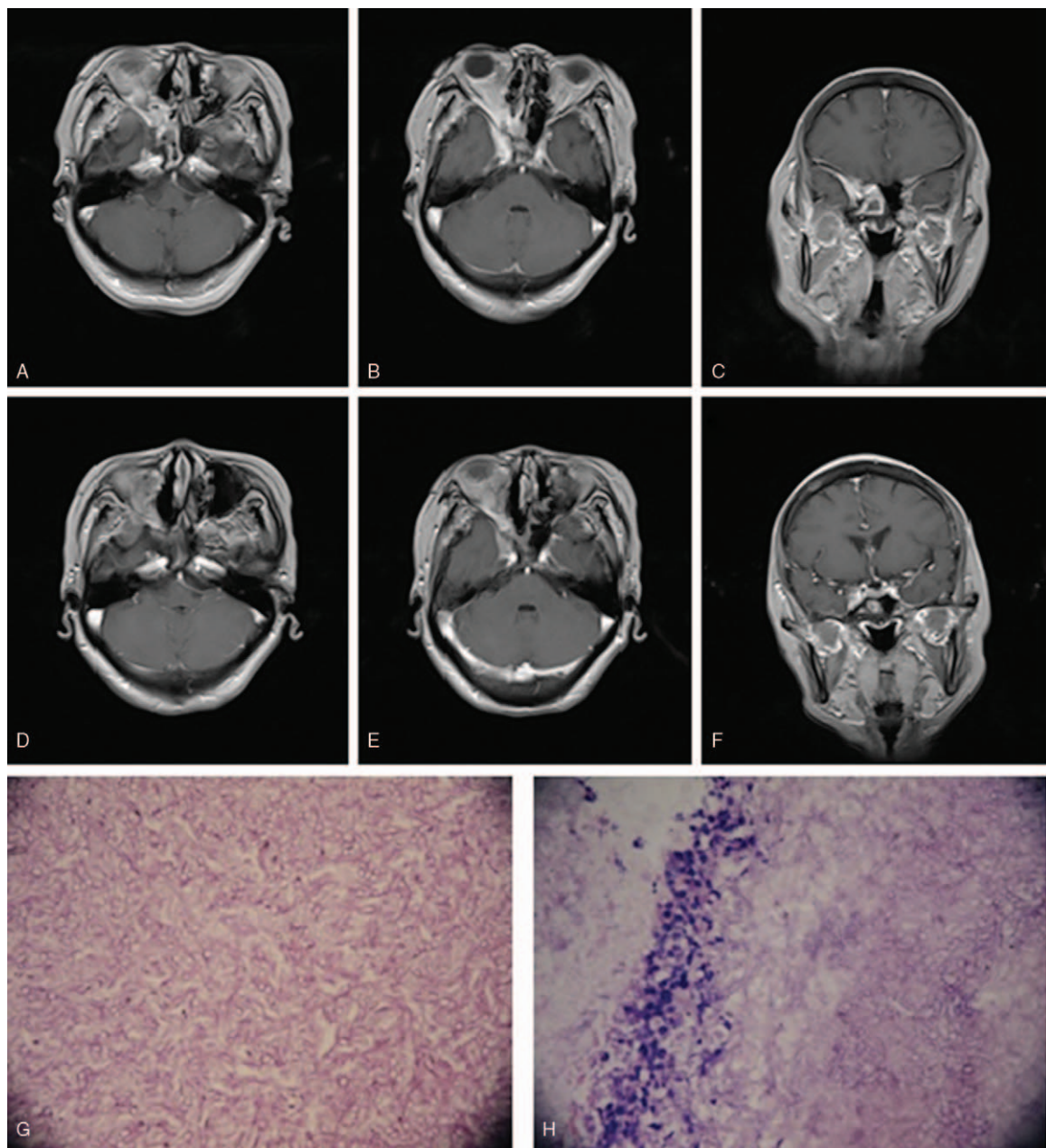
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## 2. Case report

A 64-year-old woman was admitted to the hospital with a 3-month history of headache and a 1-week history of sudden decreased vision in the right eye. Before admission, the patient began to have headaches on the right side, persistent sharp pain and nasal obstruction. The diagnosis of rhinosinusitis was considered before hospital admission, and right sphenoidotomy and partial right upper turbinectomy were performed but never completely resolved her symptoms. One week before admission, the patient experienced sudden blindness in her right eye, and the pain intensified. She had a history of poorly controlled diabetes mellitus. The clinical examination indicated right periorbital cephalalgia, right trigeminal neuralgia and right ophthalmoplegia.



**Figure 1.** A–C. Axial and sagittal T1 contrast-enhanced MRI scan showing a right orbital apex mass abutting the cavernous sinus, sphenoid sinus and posterior ethmoid sinus. D–F. Axial and sagittal T1 contrast-enhanced MRI scan (4 months after surgery) showing residual inflammatory and infective changes at the right orbital apex immediately anterior to the cavernous sinus. G–H. Microscopically, microabscesses (A–B) can be seen to contain radiating septate hyphae with angular branching hyphae (original magnification  $\times 400$ ). MRI = magnetic resonance imaging.

Axial and sagittal T1 contrast-enhanced magnetic resonance imaging (MRI) showed a right orbital apex mass abutting the right maxillary sinus, posterior ethmoid sinus, sphenoid sinus, and cavernous sinus (Fig. 1A–C). A cerebrospinal fluid (CSF) analysis revealed elevated protein levels (0.81 g/L); however, no infectious agent was found. Routine blood tests, CSF tests and IgG and IgM tests were negative. Tests for the tuberculosis antibody, HIV, fungal D-glucan, and procalcitonin were all negative. Members of the Otorhinolaryngology and Ophthalmology Departments were consulted, and functional endoscopic sinus surgery was performed. Upon debridement of the anterior face of the sphenoid sinus, it was discovered to be filled with a

light tan substance with a consistency similar to that of peanut butter. The inflamed tissue was sent to the pathology laboratory for identification. The pathology results showed septate hyphae branching at right angles, which was highly suggestive of aspergillus (Fig. 1G–H). The patient was prescribed systemic voriconazole and intravenous heparin postoperatively. Her condition improved significantly, with complete resolution of headaches, and she was discharged on daily warfarin with a goal INR of 2–3. She also received 4 months of voriconazole treatment (200 mg twice daily). At the latest follow-up, 4 months after surgery, the patient was clinically stable, and their extraocular movement had continued to improve but with persistent poor

visual acuity of her right eye and no light perception. A follow-up MRI scan 4 months after surgery showed improvement of the inflammation in the right orbital apex and cavernous sinus (Fig. 1D–F). No signs of recurrence of the disease were present.

### 3. Discussion

The main manifestations of cavernous sinus-orbital apex syndrome are orbital pain, chemosis, vision decline, and ophthalmoplegia.<sup>[8,9]</sup> Common causes include thrombosis, carotid-cavernous fistula, pituitary tumor, and infection.<sup>[10]</sup> A fungal infection spreading from the paranasal sinus to the cavernous sinus and orbital apex is a rare and potentially life-threatening disease.<sup>[8,9]</sup> In our experience, aspergillus infections usually invade the cavernous sinus or orbital apex, but rarely both. In this case, the right side of the cavernous sinus extended to the orbital apical tissue, with rapid visual decline and irreversible changes in visual acuity.

Aspergillus is a conditionally pathogenic fungus that is found in a wide range of organisms and exists in soils, water, and decaying plants. Inhalation of aspergillus spores released into the atmosphere is the typical route of infection.<sup>[4]</sup> Aspergillus infections are usually divided into noninvasive and invasive infections, and invasive aspergillosis can spread hematogenously to any organ system. The digestive tract, genitourinary system, blood vessels and CNS are the most common sites of the spread of the infection.<sup>[4]</sup> Intracranial aspergillus infection from direct infection of the adjacent paranasal sinus tissue accounts for 76% of CNS aspergillosis. Early sinus infections are often confined to the maxillary sinus and sphenoid sinus.<sup>[11]</sup> Intracranial aspergillosis can cause chronic meningitis or brain abscesses. Mycelia can penetrate the blood vessels, causing vasculitis, thrombosis, microaneurysms, and brain ischemia and necrosis.<sup>[4]</sup> This patient had a history of diabetes with poor control. The disease progressed rapidly, and the final pathological biopsy confirmed aspergillosis.

The patient's clinical manifestations, signs and imaging examinations rapidly led to the diagnosis of cavernous sinus syndrome combined with orbital apex syndrome. MRI showed the location of the lesions, and sinus CT detected bone destruction. However, the imaging studies could not exclude the possibility of tumors or infection of the saddle area. Therefore, imaging examinations lack specificity for the diagnosis of the disease.<sup>[3,10]</sup> During the course of the disease, the patient had no signs of infection, such as fever, and the laboratory tests did not provide information on which to base a diagnosis of infection. Reports have shown that when patients have decreased visual acuity and eye signs, aspergillus infection<sup>[12]</sup> should be highly suspected.

The patient underwent functional endoscopic sinus surgery before admission. We considered the possibility of infection and treated the patient with vancomycin, ceftriaxone, and metronidazole combined with low molecular weight heparin sodium for 1 week; the symptoms were not relieved. A biopsy of the lesion tissue was obtained surgically to investigate the nature of the lesion. During the second operation, a large number of brown fungus-like specimens were observed in the sphenoid and posterior ethmoid sinus in addition to sinus mucosal swelling and adjacent bone destruction, affecting the surrounding orbital apex and other tissues. The fungus-like samples and sphenoid sinus lesions were submitted for examination and showed the presence of aspergillus. The postoperative diagnosis was fungal sinusitis (right, invasive) and right cavernous sinus-orbital apex syndrome.

Surgery can quickly determine the nature of the lesion and, at the same time, allow debridement, which is crucial.<sup>[12,13]</sup> Surgical removal of the source of the infection can quickly reduce the symptoms. At the same time, after functional endoscopic sinus surgery, the inflammatory secretions in the paranasal sinus are drained. This draining reduces the anaerobic state of the paranasal sinus and prevents infection by other bacteria. There is no standard surgical treatment for orbital and cavernous sinus aspergillosis.<sup>[12]</sup> The literature has shown that to prevent inflammatory tissue from compressing the intracranial nerve or prevent invasion of the optic nerve by inflammatory tissue, it is necessary to carry out an expanded surgical debridement, such as an eyelid lateral incision.<sup>[12]</sup> This patient had extensive lesions, affecting the cavernous sinus, apex and optic nerve; intraoperative optic nerve edema; and adjacent bone destruction. The surgeons believed that expanding the scope of debridement might cause CSF leakage or increase the risk of secondary infection. Therefore, most but not all of the lesions were debrided.

The first-line treatment for chronic CNS Aspergillosis is voriconazole. The patient was prescribed systemic voriconazole and intravenous heparin postoperatively. She improved significantly with the complete resolution of her headache. At the latest follow-up, 4 months after surgery, the patient was clinically stable but showed persistent poor visual acuity of her right eye with no light perception. MRI showed improvement of the inflammation of the right orbital apex and cavernous sinus. The patient also received 4 months of voriconazole treatment. Oral voriconazole was stopped once the patient achieved a stable clinical condition. At the last follow-up, no signs of recurrence of the disease were present.

This case report presents a rare but serious complication of invasive aspergillosis rhinosinusitis, namely, cavernous sinus syndrome combined with orbital apex syndrome. Due to a lack of specific clinical, biological and radiological signs, the diagnosis of this condition remains particularly difficult. When clinicians receive patients who have experienced vision loss and have orbital signs, orbital apex aspergillosis should be highly suspected.<sup>[12]</sup> Prospective studies are needed to estimate the effectiveness of adjuvant therapies (anticoagulation and antifungal) vs surgery alone. Early surgical debridement is crucial to confirm the diagnosis and prevent mortality.<sup>[7]</sup>

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