CASE REPORT

Orbital apex syndrome secondary to acute invasive fungal rhinosinusitis diagnosed by transnasal endoscopic biopsy of the optic canal : A case report

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Abstract : Orbital apex syndrome (OAS) is a complex condition characterized by visual loss, diplopia, and eye pain that occurs secondary to several pathological processes involving the orbital apex. We report a case of acute invasive fungal rhinosinusitis (AIFRS) associated with OAS. A 76-year-old man with left-sided visual loss, diplopia, palpebral ptosis, and headache was diagnosed with OAS secondary to Tolosa-Hunt syndrome and received systemic corticosteroid therapy from his neurologist. Owing to persistent symptoms, we opened the optic canal using a transnasal endoscopic approach for a surgical biopsy of the orbital apex lesions. Histopathological evaluation revealed numerous *Aspergillus* organisms in the biopsied granuloma. After surgical debridement, he received a 12-month course of voriconazole, and no recurrence of AIFRS occurred during 8-year follow-up. Patients with OAS may occasionally be prescribed corticosteroids because the clinical manifestations of AIFRS-induced OAS are similar to those observed in OAS secondary to Tolosa-Hunt syndrome, especially no nasal symptoms which is known to respond to corticosteroid therapy. Because both AIFRS-induced OAS and OAS secondary to Tolosa-Hunt syndrome induce ophthalmoplegia, proptosis, eye pain, it is sometimes difficult to differentiate these two diseases in early stage. However, corticosteroid therapy causes exacerbation of fungal infection in patients with AIFRS-induced OAS resulting in delayed accurate diagnosis and poor prognosis. AIFRS is associated with a high mortality rate ; therefore, transnasal endoscopic biopsy of orbital apex lesions before corticosteroid administration is recommended in patients with OAS. J. Med. Invest. 71 : 310-313, August, 2024

Keywords **:** *orbital apex syndrome, transnasal endoscopic approach, acute invasive fungal rhinosinusitis, Aspergillus, voriconazole*

INTRODUCTION

Orbital apex syndrome (OAS) is a complex condition that involves simultaneous dysfunction of the optic nerve (II) in the optic canal, and the oculomotor (III), trochlear (IV), abducens (VI), and the ophthalmic branch of the trigeminal nerve (V1) in the superior orbital fissure at the orbital apex. OAS is characterized by visual loss, diplopia, and eye pain and is caused by several pathological processes, including inflammation, infection, neoplasm, trauma, or vascular disease (1, 2).

Acute invasive fungal rhinosinusitis (AIFRS) is an opportunistic infection in patients with hematological malignancies, chronic immunosuppression, and poorly controlled diabetes mellitus. Reportedly, patients with AIFRS show poor prognosis, and early and accurate diagnosis are important for a favorable prognosis (3). Early surgical debridement and antifungal therapy are recommended for treatment of AIFRS (3).

We report a case of AIFRS in a patient with OAS who presented with left visual loss, diplopia, left palpebral ptosis, and headache. Computed tomography (CT) and contrast-enhanced magnetic resonance imaging (MRI) revealed a mass along the left optic nerve canal extending to the left posterior ethmoid sinus and the left cavernous sinus. He was diagnosed with left OAS due to Tolosa-Hunt syndrome and administered corticosteroid by a neurologist ; however, the patient's symptoms did not improve. We opened the optic canal via a transnasal endoscopic approach and performed surgical debridement, followed by the administration of voriconazole (VRCZ). In this case, AIFRS induced OAS with visual loss and eye pain becoming worse after steroid therapy, resulting in the extended duration required to reach a diagnosis and poor prognosis of visual function even though opening the optic canal followed by antifungal therapy.

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CASE REPORT

A 76-year-old man who had no medical history presented with left-sided visual loss. He was diagnosed with left optic neuritis by an ophthalmologist and received oral betamethasone 1.5-3.0 mg/day for 1 month. However, his visual loss did not improve, and he developed diplopia, left palpebral ptosis, and headache, a month later. Contrast-enhanced MRI revealed a mass along the left optic canal extending to the left cavernous sinus, and he was diagnosed with left OAS by a neurologist. He received 3-day methylprednisolone 1000 mg/day corticosteroid pulse therapy for diagnostic and therapeutic purposes for OAS secondary to Tolosa-Hunt syndrome ; however, his symptoms stayed the same. Finally, the patient visited our hospital for surgical biopsy of the left orbital apex lesions, 2 months after the onset of initial visual symptoms. At his first visit, he presented with facial pain, and examination revealed left-sided ptosis and loss of the light reflex with visual acuity restricted to only light perception in his left eye. Left ocular movements were limited in all directions. Nasal endoscopy did not show rhinorrhea, mucosal necrosis, or a tumor.

CT revealed a mass of soft tissue density without an internal

high-density area along the left optic canal extending to the left posterior ethmoid sinus and the left cavernous sinus. CT also revealed bony destruction between the optic canal and the skull base (Fig. 1). MRI revealed a mass with an isointense signal on T1-weighted and a low-intensity signal on T2-weighted imaging, extending along the left optic canal to the left posterior ethmoid sinus and the left cavernous sinus. Contrast-enhanced MRI revealed enhancement of the dura mater at the point of contact with the mass (Fig. 2).

Blood test results showed normal white blood cell, as well as serum C-reactive protein, glucose, and glycosylated hemoglobin levels. The serum β-D glucan level was <6.0 pg/mL (normal <6.0 pg/mL), and the *Aspergillus* antigen test showed negative results. Serum C3, C4, and CH50 levels were normal. Proteinase 3 anti-neutrophil cytoplasmic antibodies and myeloperoxidase-anti-neutrophil cytoplasmic autoantibodies were negative. The soluble interleukin-2 receptor and squamous cell carcinoma antigen were normal. Cerebrospinal fluid evaluation did not show an increase in the number of cells or protein levels, and bacterial culture test results were negative.

We performed a surgical biopsy of the orbital apex lesion via a transnasal endoscopic approach. We detected a primary lesion along the optic canal extending to the left posterior ethmoid sinus. We used intraoperative rapid histopathological diagnosis at two sites and reveal the findings below. Histopathological examination of a mucosal biopsy specimen obtained over the optic canal in the left posterior ethmoid sinus showed only mucosal inflammation (Fig. 3a). After removing the inflammatory mucosa, a soft white granuloma was detected in the optic canal (Fig. 3b). Histopathological examination of the granuloma revealed numerous Aspergillus organisms with characteristic branching septate hyphae (Fig. 4). After intraoperative rapid diagnosis, we decided to opened the optic canal further from the orbital apex to the skull base and completely removed the granulomatous lesions along the optic canal including those at the optic nerve sheath macroscopically, with preservation of optic nerve. He was diagnosed with *Aspergillus*-induced AIFRS, which led to OAS and received intravenous antifungal therapy with VRCZ immediately postoperatively. His facial pain gradually improved immediately, and ptosis and limitation in ocular movements disappeared 2 months postoperatively. However, visual acuity did not recover. The patient received VRCZ intravenously for 1 month, followed by an oral course for 1 year. Nasal endoscope (Fig. 5a) and MRI (Fig. 5b, c) showed no recurrence of AIFRS. No recurrence of AIFRS was observed over 8-year follow-up. We obtained informed consent for both the procedure and the publication.

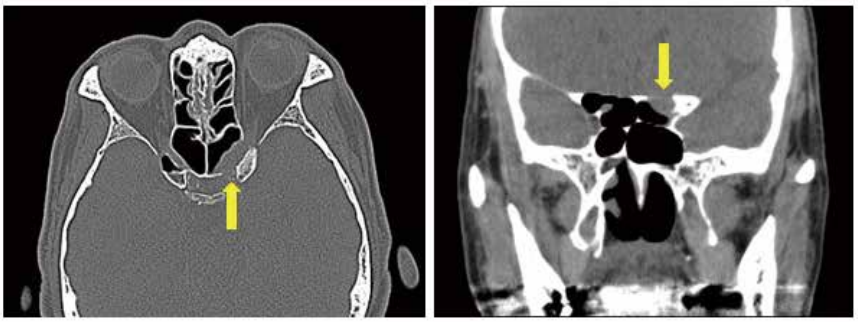

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Figure 1. Axial CT scan (a) showing a mass of soft tissue density along the left optic canal extending to the left posterior ethmoid sinus and the cavernous sinus (arrow). Coronal CT scan (b) showing bony destruction between the optic canal and the skull base (arrow).
CT : computed tomography

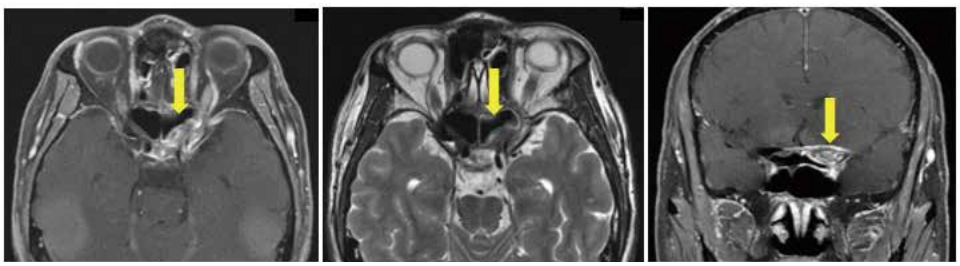

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Figure 2. Contrast-enhanced axial MRI scan showing a mass with contrast enhancement (a) and a low-intensity signal on a T2-weighted image (b) along the left optic canal extending to the left posterior ethmoid sinus and the cavernous sinus (arrow). Contrast-enhanced MRI scan (c) showing enhancement of the dura mater at the point of contact with the mass (arrow).
MRI : magnetic resonance imaging

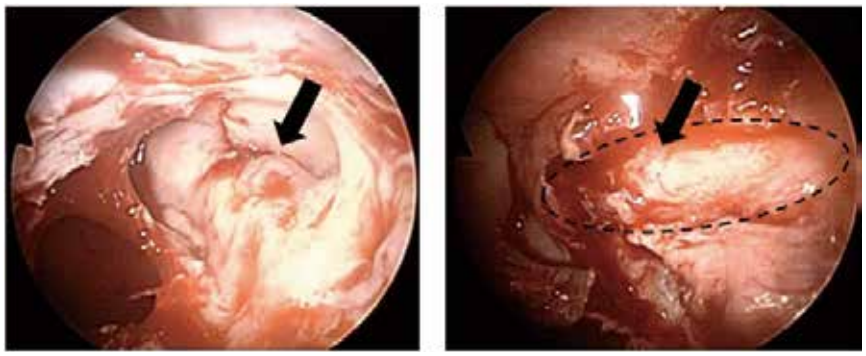

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Figure 3. Image showing an endoscopic view of the left-sided posterior ethmoid sinus. A primary lesion (arrow) (without evidence of fungal infection) is observed along the optic canal (a). A soft white granuloma (arrow) (with organisms consistent with *Aspergillus*) is observed within the opened optic canal (b). The range of opening optic canal was showed by dotted circle.

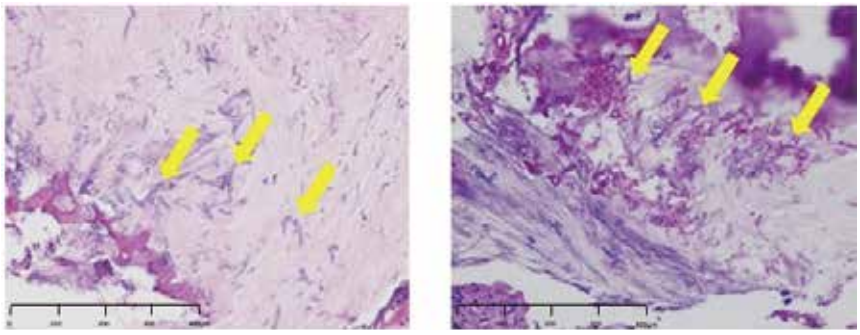

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Figure 4. Histopathological findings of the biopsied granuloma. Specimens of the biopsied granuloma stained using hematoxylin-eosin (arrow) (a) and periodic acid-Schiff stain (arrow) (b) showing numerous *Aspergillus* organisms with characteristic branching septate hyphae.

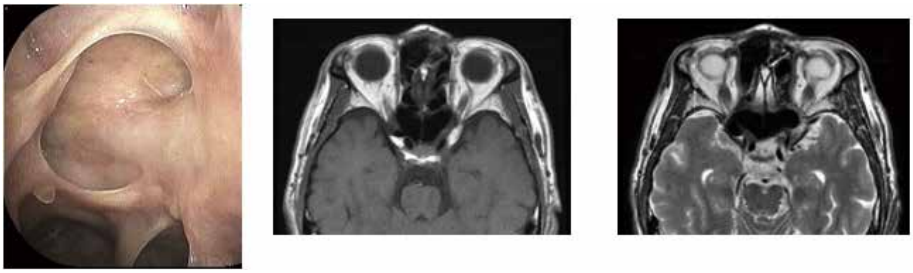

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Figure 5. Postoperative endoscopic view of the left-sided posterior ethmoid sinus (a) and MRI scans of T1-weighted image (b) and T2-weighted image (c) showing no recurrence of AIFRS.

DISCUSSION

We report a case of OAS secondary to AIFRS who presented with left visual loss, diplopia, left palpebral ptosis, and headache. Our patient was administered corticosteroids for diagnostic and therapeutic purposes for OAS secondary to Tolosa-Hunt syndrome before he visited our department because the clinical manifestations of AIFRS-induced OAS are similar to those of OAS secondary to Tolosa-Hunt syndrome, which responds well to systemic corticosteroid therapy. However, reportedly corticosteroid therapy causes exacerbation of fungal infection in patients with AIFRS-induced OAS and often results in delayed accurate diagnosis and poor prognosis (4, 5), which is attributed to corticosteroid-induced immunosuppression with a consequent increase in the pathogenicity of *Aspergillus* and an increased growth rate of *Aspergillus* (6). Therefore, corticosteroids should not be used for patients with OAS before accurate diagnosis. Although there are no specific clinical signs of AIFRS, symptoms such as facial swelling, fever, ophthalmoplegia, proptosis, visual loss, severe facial pain and headache have been reported to suggest AIFRS (7).

Although the serum β-D glucan level is a useful diagnostic marker of sino-orbital aspergillosis , its sensitivity is low in cases of localized aspergillosis (8). In fact, our patient with typical OAS

symptoms showed normal serum β-D glucan levels.

Accurate diagnosis of AIFRS requires surgical biopsy of the lesion (1). However, surgical biopsy of a lesion at the orbital apex is technically challenging in patients with OAS owing to the anatomical complexity of this area. Previous studies have reported a transcranial open biopsy for orbital apex lesions (9) ; however, this procedure is often associated with serious complications, such as seizures, strokes, blindness, and cerebrospinal fluid leakage (10). Lately, compared with the conventional external approach for orbital apex lesions, transnasal endoscopy is shown to offer several advantages, including less invasiveness, better visualization, lesser pain, and no facial scarring (10). Therefore, we performed transnasal endoscopic biopsy in our patient with OAS, followed by histopathological evaluation, which showed *Aspergillus* in the biopsied granuloma in the optic canal, which led to a diagnosis of AIFRS-induced OAS associated with *Aspergillus*.

AIFRS is a fatal condition with an overall mortality rate of approximately 50% (7). It has been reported that the case of AIFRS-induced OSA were treated with systemic steroids due to a misdiagnosis of Tolosa-Hunt Syndrome, leading to fatal outcomes (4). Advanced age, intracranial involvement, and non-surgical debridement were identified as negative prognostic factors associated with this condition (7). Complete removal of lesions by extensive surgery through external incision, followed by concurrent administration of systemic antifungal agents was recommended for the treatment of AIFRS (3, 11). However, in the current study, we observed that compared with external incision surgery, endoscopic surgery significantly improved disease-specific survival (7, 12).

Currently, VRCZ is recommended as the first-line antifungal drug for AIFRS based on the results of a previous study in which compared with amphotericin, VRCZ significantly improved survival outcomes (13), as well as outcomes of central nervous system aspergillosis (14). The median duration of antifungal drug administration was 60 days (15). Japanease Guidelines for Management of Deep-seated Mycosis show that treatment is usually required for at least 6–12 weeks in patients with a good clinical course and that treatment continuation is necessary in patients with persistent immunosuppression or in those with an unfavorable clinical course (3). Our patient received a 12-month course of VRCZ after surgical debridement because of advanced age and intracranial involvement, and survived with no recurrence of mycosis during 8-year postoperative follow-up.

In conclusion, we report a case of OAS secondary to AIFRS with *Aspergillus* that was diagnosed using endoscopic surgical biopsy after opening the optic canal via the transnasal approach. The patient was successfully treated with endoscopic surgical debridement from the orbital apex to the skull base and antifungal therapy using VRCZ without recurrence during 8-year follow-up, although visual acuity did not recover. It is sometimes difficult to differentiate Tolosa-Hunt syndrome in early stage. However, AIFRS is associated with a high mortality rate ; therefore, corticosteroids should not be used for diagnostic and therapeutic purposes before performing a less invasive transnasal endoscopic biopsy of orbital apex lesions for accurate diagnosis in patients with OAS.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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