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# A Case of Invasive Sphenoid Sinus Aspergillosis Presenting as Oculomotor Nerve Palsy in a Healthy Patient

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## Abstract

**Invasive sphenoid sinus aspergillosis is a rare infection and usually affecting immunocompromised patients. We describe an invasive sphenoid sinus aspergillosis patient with immunocompetent who present progressive ocular dysfunctions. A 66-year-old woman with no history of immune dysfunction was referred to our hospital with orbital complications. Computed tomography (CT) scan and magnetic resonance imaging (MRI) showed a mass lesion extending from the left orbital apex to the sphenoid sinus. Inflammatory diseases were not suspected by laboratory findings, but a transnasal endoscopic biopsy revealed sphenoid sinus aspergillosis. After treatment of antifungal medication, this patient showed improvement and no sign of recurrence during the follow-up period. Diagnosis of invasive sphenoid sinus aspergillosis in an immunocompetent, healthy individual, was challenging. However, if patients have sinus wall deformities and orbital complications, early surgery is necessary to improve their prognosis.**

Keywords: sphenoid sinus aspergillosis, immunocompetent patient, endoscopic biopsy

## Introduction

Paranasal sinus aspergillosis is mostly observed in patients who are immunocompromised due to the use of immunosuppressants or steroids. The non-invasive type localized in the paranasal sinus is common, but occasionally, invasive paranasal sinus aspergillosis invading the cavernous sinus, the orbit, or the central nervous system may develop. If the surgery is not performed, the prognosis is extremely poor.[1)]

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Here, we report a case of invasive sphenoid sinus aspergillosis in an immunocompetent, healthy individual, where establishing the definitive diagnosis was challenging.

## Case Report

The patient was a 66-year-old woman with no history of immune dysfunction. Her family history was unremarkable. The patient was aware of pain in the left maxilla for 2 months. As she presented ptosis and diplopia on the left side, she visited an ophthalmologist. Left oculomotor nerve and left abducens nerve palsy were identified, and the patient was referred to an otolaryngologist. A head computed tomography (CT) scan was performed for further examination and a mass lesion extending from the left orbital apex to the paranasal sinus was revealed.

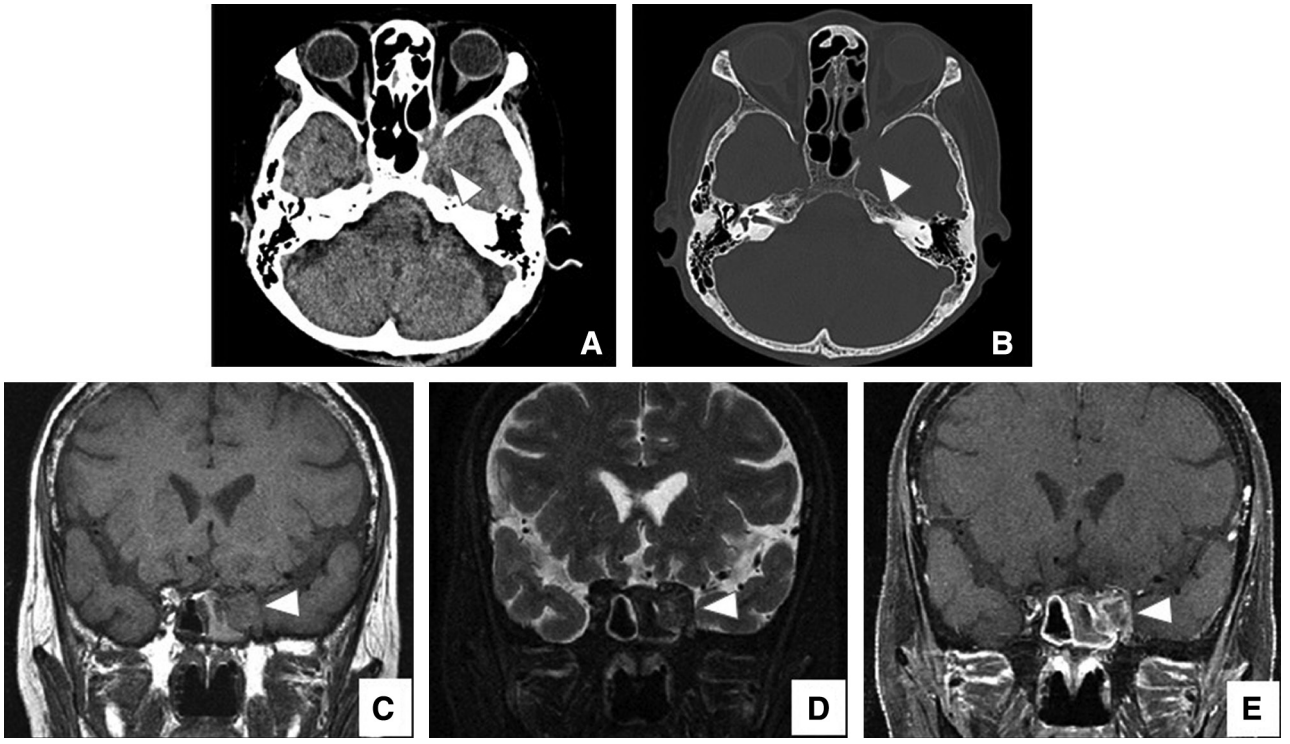


**Fig. 1 CT demonstrated that erosion of the lateral wall of the left sphenoid sinus with extension to the orbit (A, B). The MRI showed an isosignal intensity on the T1-weighted image (C) and a low signal on the T2-weighted image in the left sphenoid sinus (D). The expansile lesion is seen in the sinus with abnormal enhancement (E). CT: computed tomography, MRI: magnetic resonance imaging.**

Blood tests were performed, but no signs of inflammation were noted, and Aspergillus and β-D glucan antigen tests were negative. Tolosa–Hunt syndrome was suspected, and steroid treatment was administered. However, symptoms did not improve, and the patient became aware of left vision impairment. The patient was referred to our department for further examination.

On admission, she was alert, but she had loss of light perception, ptosis, pupil dilation, loss of light reflex in her left eye, and left ocular motility disturbance; medial gaze, up gaze, and down gaze were all 1/5, and lateral gaze was 0/5. She had no sensory abnormality in the face, and there were no intranasal findings. Laboratory findings on admission included a leukocyte count of 4500/mm$^3$, a C-reactive protein of 0.10 mg/dL, and no other notable findings. A plain CT scan of the head revealed a mass lesion, extending from the cavernous sinus to the orbit on the left, and erosion in the sphenoidal sinus (Figs. 1A and 1B). Magnetic resonance imaging (MRI) revealed that the lesion was isointense on T1-weighted imaging and mostly hypointense on T2-weighted imaging, though partially hyperintense (Figs. 1C and 1D). The contrast effect was heterogeneous (Fig. 1E).

Because it was difficult to differentiate a neoplasm from an infection based on the imaging and laboratory results available, a transnasal endoscopic biopsy was performed. The tumor protruded into the left side of the sphenoidal sinus and was whitish elastic soft, and hemorrhagic. Erosion of the inner wall of the cavernous sinus was observed (Figs. 2A and 2B). Histopathological findings confirmed the presence of hyphae, indicating a suspicion of aspergillosis (hematoxylin and eosin staining: Fig. 2C, Grocott's staining: Fig. 2D). The patient was diagnosed with invasive paranasal sinus mycosis, and intravenous injection of liposomal amphotericin B (L-AMB) was initiated. *Aspergillus fumigatus* was detected in the cultured specimen, and a definitive diagnosis of sphenoid sinus aspergillosis was made. After the definitive diagnosis, L-AMB was changed to voriconazole (VRCZ), with micafungin sodium (MCFG) and intranasal amphotericin B (AMPH-B). Symptoms did not worsen, and her ocular motility disturbance was improved.

## Discussion

Paranasal sinus disease often has one major lesion in the ethmoidal or the maxillary sinus. Lesions in

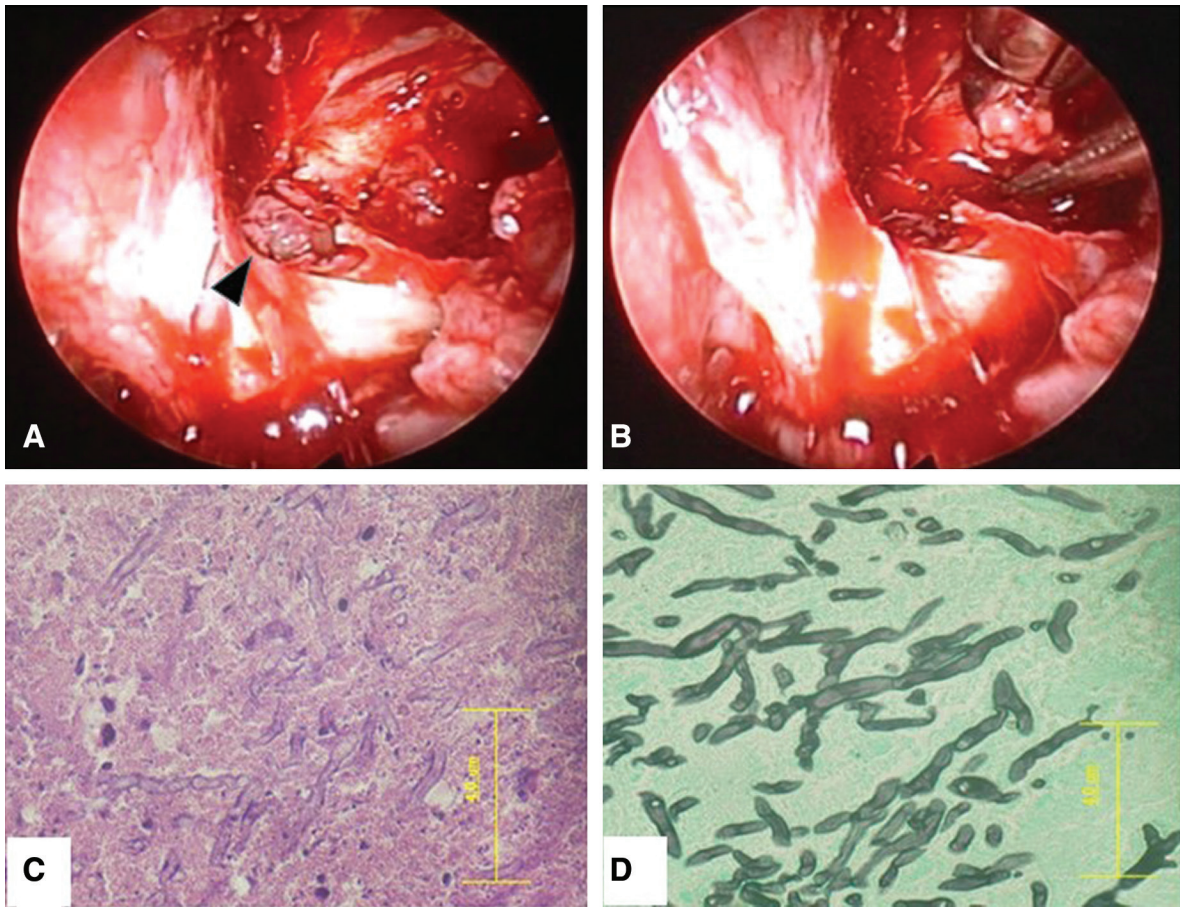


**Fig. 2 Intraoperative view of left sphenoid sinus: Whitish elastic soft, and hemorrhagic tumor was removed. Erosion of the inner wall of the cavernous sinus was observed (A, B). Histopathologic specimen showed typical fungal hyphae, indicating a suspicion of aspergillosis, on hematoxylin–eosin staining (C) and Grocott's staining (D).**

the sphenoidal sinus are also common, but it is rare to see the lesion localized to the sphenoid sinus.[2] In case the lesion is localized in the sphenoid sinus, characteristic symptoms include headache and ocular symptoms, whereas nasal congestion and rhinorrhea are rare[3]; therefore, patients typically visit a neurologist for the first medical consultation. Diseases with the main lesion in the sphenoid sinus are usually inflammatory diseases or tumors, whereas mycoses are rare. Many cases of mycosis in the sphenoid sinus are caused by Aspergillus and often in the wake of immunosuppression due to administration of immunosuppressants, including steroids. The mechanism of the infection in immunocompetent patients is not clearly understood, but the number of immunocompetent patients has been increasing. Recent studies have suggested that they can be caused by low nutrition and diabetes.[4] Sphenoid sinus aspergillosis is classified into the non-invasive type, where the focal infection remains in the paranasal sinus with a favorable prognosis, and the invasive type, which has a poor prognosis and where vascular invasion and bone destruction occur. Most cases are the non-invasive type. However, when the lesion is in the sphenoid sinus, the cavernous sinus and ocular nerves can be invaded, which facilitates invasiveness; thus, its prognosis tends to be worse than other cases involving the paranasal sinus.[5] Invasive sphenoid sinus aspergillosis causes various neuropathic symptoms associated with invasion of the skull base. In many cases, the ocular nerves, the orbital apex, and the cavernous sinus are invaded, leading to oculomotor nerve palsy, abducens nerve palsy, and visual impairment. In the present case, invasion extended to the orbital apex and the cavernous sinus, resulting in the above-mentioned symptoms. Symptom deterioration may reflect vascular invasion, and cerebral infarction can develop due to a mycotic aneurysm and vascular occlusion.

In the early stage, invasive sphenoid sinus aspergillosis does not give rise to many symptoms.

Likewise, CT and MRI image results are initially nonspecific. Therefore, in many cases, establishing the diagnosis at an early stage is challenging.[6] However, fungal infections, including aspergillosis, should be considered in cases of paranasal sinus lesions, as a delay in diagnosis can lead to a poor prognosis. CT findings in invasive sinus aspergillosis include heterogeneity within the mass, bony destruction images, and calcification, but they are nonspecific when compared to MRI. Decreased signal intensity of T1-weighted and extremely low signal on T2-weighted images are specific MRI findings.[4,7] The initial CT findings of this case did not show internal heterogeneity and bone destruction, but it did appear at the time of symptom progression. It is suggested that as the infection progresses, the imaging findings may become more typical, and it is important to follow-up the imaging closely. If the lesion is localized in the sphenoid sinus, inflammatory disease or neoplastic lesions are mostly suspected, whereas mycosis is not. In addition, the patient in the present case was not immunodeficient, and at the first examination, none of the test results indicated local or systemic inflammation. Antigen tests for Aspergillus and β-D glucan were also negative. These results made it even more difficult to establish a diagnosis. However, the present case showed invasion of the cavernous sinus, the biopsy should have been performed at an early stage to establish a definitive diagnosis.

Treatment of invasive sphenoid sinus aspergillosis involves surgical removal of the focal infection and administration of an antifungal agent. Although cases that are difficult to treat by operation are supposed to have extremely poor prognosis, in recent years, with the combined use of antifungal agents, successful cases of conservative treatment are no longer rare. In the present case, after the definitive diagnosis based on the positive culture result, intravenous administration of VRCZ (300mg/day) and MCFG (300mg/day) and intranasal AMPH-B were initiated. One month of MCFG treatment and 4 months of VRCZ treatment were administered. There was no recurrence of the infection on imaging findings and symptoms did not worsen at 6 months. Although AMPH-B has long been the gold standard in invasive paranasal sinus aspergillosis, VRCZ has recently outperformed AMPH-B and is the first-line treatment. There are no definite criteria for termination of treatment, at least 4 weeks of antifungal medication is recommended.

In lesions located in the sphenoid sinus and invading the cavernous sinus, invasive paranasal sinus mycosis should not be excluded even if blood tests fail to provide the evidence for fungal infection. Until a definitive diagnosis is made, the use of steroid should be avoided, and biopsy should be performed at an early stage. It should also be noted that for the definitive diagnosis, not only histopathological findings but also proof of the causative microorganism by direct isolation in culture is necessary. Surgical resection is recommended for better clinical outcomes, but most patients are immunocompromised and require careful selection of treatment options. Endoscopic endonasal transsphenoidal approach is useful because it is less invasive to the patient and allows for the identification of fungal ball. Complete removal of the lesion is important to prevent recurrence, and adequate washing and drainage of the infected cavity is especially important as extension into the cavernous sinus can cause severe thrombosis.[7] Prompt release of optic nerve compression is also recommended, as visual disturbances in patients have poor treatments outcome in restoring vision.[8]

## Conclusions

We reported a case of invasive sphenoid sinus aspergillosis in a healthy patient without immunodeficiency. At the initial examination, fungal antigen test for Aspergillus was negative and the increase in β-D glucan concentration was not observed. Thus, the diagnosis of this case was difficult. Sphenoid sinus aspergillosis can develop even in the absence of immunosuppression. In case fungal infection is suspected on imaging, a biopsy by endoscopic endonasal transsphenoidal approach, including surgical resection should be performed at an early stage to diagnose it histopathologically and microbiologically.

## Conflicts of Interest Disclosure

No authors report any conflicts of interest.

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