Invasive fungal sinusitis of isolated sphenoid sinus in immunocompetent subjects

Hemant Chopra,1 Kapil Dua,1 Vineeta Malhotra,2 Rishi Pal Gupta1 and Harpreet Puri2
Departments of 1ENT and 2Pathology, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Summary
Invasive fungal sinusitis of the paranasal sinuses in a healthy immunocompetent person is uncommon. Isolated involvement of any paranasal sinus, particularly sphenoid sinus is rare. In this study, five immunocompetent patients who had no nasal complaints but obscure symptoms of headache and orbital symptoms such as diplopia, retro-orbital pain and loss of vision were diagnosed to be having fulminant fungal sinusitis of the sphenoid sinus. Three patients had aspergillosis and two patients had mucormycosis. These patients initially presented to neurologists and ophthalmologists because they had no ENT complaints. The diagnosis was made on endoscopy, radiology and histopathology. They were treated aggressively according to the standard protocols. The purpose of this paper is to bring to light the changing clinical spectrum of invasive fungal sinusitis. It can occur in immunocompetent patients and in the form of isolated sphenoid sinus involvement.

Key words: amphotericin B, aspergillosis, itraconazole, surgery.

Introduction
Fulminant infection of the nose and paranasal sinuses in an immunocompromised patient by mucormycosis is a well-known entity. But the spectrum of fungal disease is changing. Aspergillosis, which is saprophytic and ubiquitous in nature, is now known to cause massive destruction of paranasal sinuses in immunocompromised as well as immunocompetent patients.

The suspicion of aspergillosis arises whenever a patient of chronic maxillary sinusitis does not respond to the usual conservative therapy,1 but the chances of isolated sphenoid sinus involvement are very less. It is because of the anatomic location of the sphenoids and the decreased nasal airflow in that area.2 The symptoms in these patients are different such as headache, retro-orbital pain, diplopia, exophthalmos and blindness. This is because of the rapidly progressive gangrenous necrosis of the mucoperiosteum advancing relentlessly to cause early destruction of the bony walls of sphenoid sinus and involvement of the surrounding important structures.1 Because of their insidious onset, frequently resulting in missed and delayed diagnosis, sphenoid sinus lesions are a potentially lethal medical condition.3

The cases presented in this study show the changing spectrum of invasive fungal sinusitis (aspergillosis and mucormycosis) in the immunocompetent patients as none of our patients were immunocompromised and had no nasal problems. Also isolated sphenoid sinus involvement in fungal infections is rare,4 but our five patients had only sphenoid sinus mycosis.

Materials and methods
Five cases of invasive sphenoid sinus mycosis (Table 1) were encountered in our institution in a 3-year period of 2002–2004. The patients initially presented to neurologists and ophthalmologists for headache and visual complaints were diagnosed to have invasive sphenoid sinus aspergillosis in three and invasive mucor in two cases on ENT cross consultation. A detailed otorhinolaryngological and systemic workup was done. No predisposing medical illness was found in any case. None of these patients had any nasal complaints. The radiological investigations were done before ENT consultation. Non-contrast computed tomography (CT) scan and magnetic
resonance imaging (MRI) with T1 and T2 weighted images was used for assessment of the disease extent. Once the lesion of the sphenoid sinus was picked up on CT/MRI, a nasal endoscopy was planned both for diagnostic and therapeutic purposes. The diagnosis was made on histopathology, which was consistent with fungus. Postoperatively each case received amphotericin B and itraconazole (Table 2) except case 4 who receive only itraconazole because this case had no visual complaints. After a test dose, gradually a dose of 1 mg kg\(^{-1}\) was given till the maximum total dose of 2 g. At discharge itraconazole in the dosage of 200 mg b.d. was given for 2 months. All these patients were followed up regularly in ENT out-patients department (OPD).

Patients and results

Case 1

A 66-year-old female, non-diabetic was admitted to the hospital with headache and sudden loss of vision right eye. The headache was present in the right temporal region which was severe, continuous, radiating to the right side of cheeks, eye and upper jaw for the past 2 months. The vision decreased suddenly to the extent of light perception only in the right eye. No complaint of nasal discharge, blockade, decreased sense of smell, or any other nasal complaint was present. The patient had no complaint in the left eye. On clinical examination,

<table>
<thead>
<tr>
<th>Patients (case no.)/age/sex</th>
<th>Clinical features</th>
<th>Signs</th>
<th>Radiology</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 66 years (F)</td>
<td>Right temporal headache (2 months)</td>
<td>Right eye – ptosis, absent eye movements, absent pupillary reflexes</td>
<td>MRI suggestive of an ill-defined mass in the right sphenoid sinus with thickening of right optic nerve and cavernous sinus (Fig. 1)</td>
<td>Aspergillus (Fig. 2)</td>
</tr>
<tr>
<td>2. 17 years (F)</td>
<td>Left-sided headache (25 days) Progressive deterioration of vision in left eye (15 days)</td>
<td>Left eye – no vision, absent pupillary reflexes</td>
<td>MRI suggestive of an ill-defined lateral mass in the sphenoids with erosion of left sphenoid wall (Fig. 4)</td>
<td>Aspergillus</td>
</tr>
<tr>
<td>3. 32 years (F)</td>
<td>Diplopia (2 months) Headache for (1 month) Sudden loss of vision right eye (1 day)</td>
<td>Right eye – vision 6/36, normal movements</td>
<td>CT scan suggestive of soft tissue mass involving sphenoid and causing destruction of bony margins and extension into sella turcica (Fig. 6)</td>
<td>Mucor (Fig. 5)</td>
</tr>
<tr>
<td>4. 19 years (F)</td>
<td>Headache for (1 month)</td>
<td>No eye signs and symptoms</td>
<td>MRI suggestive of a well-defined mass in the sphenoid with the erosion of intersphenoidal septum</td>
<td>Aspergillus</td>
</tr>
<tr>
<td>5. 77 years (M)</td>
<td>Headache for (1 month) Decreased vision left eye (15 days)</td>
<td>Left eye – Vision 6/36, pupillary reflexes normal</td>
<td>CT scan suggestive of a well-defined mass in the sphenoid with the erosion of left lateral sphenoidal wall</td>
<td>Mucor</td>
</tr>
</tbody>
</table>

Table 1 Showing the age, sex, symptoms, signs, radiological features and histopathology of five patients.

<table>
<thead>
<tr>
<th>Patients (case no.)/age/sex</th>
<th>Surgery done</th>
<th>Amphotericin B given</th>
<th>Itraconazole given</th>
<th>Final outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 16 years (F)</td>
<td>Endoscopic sphenoidectomy</td>
<td>2 g</td>
<td>200 mg b.d. for (2 months)</td>
<td>Death after 6 months of surgery</td>
</tr>
<tr>
<td>2. 17 years (F)</td>
<td>Endoscopic sphenoidectomy</td>
<td>500 mg</td>
<td>Not given</td>
<td>Death after 1 month of surgery</td>
</tr>
<tr>
<td>3. 32 years (F)</td>
<td>Endoscopic sphenoidectomy</td>
<td>2 g</td>
<td>200 mg b.d. for (2 months)</td>
<td>Doing well till date (6 months)</td>
</tr>
<tr>
<td>4. 19 years (F)</td>
<td>Endoscopic Sphenoidectomy</td>
<td>Not given</td>
<td>200 mg b.d. for 2 months</td>
<td>Doing well till date (7 months)</td>
</tr>
<tr>
<td>5. 77 years (M)</td>
<td>Endoscopic Sphenoidectomy</td>
<td>1.5 g</td>
<td>200 mg b.d. for 2 months</td>
<td>Doing well till date (3 months)</td>
</tr>
</tbody>
</table>
there was ptosis of right eye, and eye movements were restricted in all directions. Pupillary reflexes were absent. Anterior and posterior rhinoscopy showed no abnormality in the nasal cavity. The CT scan paranasal sinuses (PNS) and MRI PNS and brain revealed an ill-defined mass in the right sphenoid sinus with thickening of right optic nerve and cavernous sinus (Fig. 1). On nasal endoscopy under local anaesthesia, the osteomeatal complex, the middle meatus and ethmoids on the right side were found to be normal. In the sphenoethmoidal recess area, the sphenoid sinus opening was blocked by cheesy material, which was removed and sent for KOH staining, fungal culture and histopathological examination. The rostrum of sphenoid and recess opening was widened with the burr. The posterior end of middle turbinate was resected to allow for the drainage of sphenoid sinus. No breach was found in the mucosal lining of sphenoid sinus. The biopsy report revealed numerous septate, dichotomous branching *Aspergillus* fungal hyphae infiltrating the epithelial lining of the sphenoid sinus (Fig. 2). After endoscopic clearance of the sphenoid sinus, there was a gradual improvement in the movement of the right eye. This led to the improvement of 2, 3, 4th cranial nerve except 6th cranial nerve, which showed partial improvement. The patient was put on amphotericin B till 2 g and discharged on Itraconazole 200 mg b.d.

On a follow-up after 4 months the patient had no headache, perception and projection of light was present and was able to move her right eye in all directions except right lateral position. On nasal endoscopy, the mucosal lining was found to be healthy in the sphenoid sinus. MRI brain and PNS showed significant improvement when compared with the previous MRI scan (Fig. 3). After 6 months the patient presented with intracranial extension of the fungus and died within 2 days of re-admission.

**Case II**

A 17-year-old female presented to us with the complaint of headache, decreased vision left eye for 25 days. The patient had headache on left side, which was continuous, severe, radiated to left eye, and was associated with vomiting (non-projectile). Ophthalmological examination revealed an absent direct and consensual light reflex of the left eye with absent perception and projection of light. Right eye was normal. CT scan
PNS and MRI nose and PNS revealed an ill-defined lateral lesion of the sphenoids with erosion of the left sphenoidal wall (Fig. 4). On nasal endoscopy, the middle turbinate was lateralised and a big, firm leathery mass filling the sphenoid sinus was visualised. Endoscopic sphenoidotomy was done under general anaesthesia. Fungating mass blocking the sphenoid sinus opening was removed. Ostium was widened and pus drained out. Hypertrophic mucosa was also removed leaving behind the healthy mucosa in sphenoid sinus. The biopsy was taken which revealed aspergillosis of the sphenoid sinus.

Postoperatively, patient reported marked improvement in symptoms of headache but no improvement in vision. The patient was started on amphotericin B and was discharged on request. She received only 500 mg of amphotericin B. The patient did not come for follow-up. After 1 month, she presented with severe headache and projectile vomiting. MRI scan revealed an intradural extension of the fungus. The patient’s condition deteriorated rapidly. She died within 24 h of re-admission.

Case III

A 32-years-old female presented with double vision in right eye for 2 months, inability to move right eye in right direction and headache mainly in the vertex for 1 1/2 months, sudden loss of vision and purulent post-nasal drip 1 day prior to admission. On clinical examination, both the nasal cavities were normal on anterior rhinoscopy but purulent discharge was seen in both choanae on posterior rhinoscopy. The ophthalmological examination revealed right lateral rectus palsy. CT scan paranasal sinuses revealed a soft tissue mass involving the sphenoid sinus. It was causing destruction of the bony margins and extending into the sella turcica (Fig. 5). On nasal endoscopy the floor, inferior turbinate and osteomeatal complex on right side were found to be normal. Dirty greenish secretions and cheesy material were found in the sphenethmoidal recess area. Endoscopic sphenoidotomy was done. The purulent secretions were removed from the sphenoid sinus and sent for histopathological examination. Inter sinus septum was found to be eroded. Pulsations of internal carotid artery were seen clearly. Dehiscent bony canal was suspected. The histopathological examination revealed invasive mucormycosis (Fig. 6). A sudden and immediate cessation of headache and improvement of vision was reported by the patient. Postoperative amphotericin B

---

**Figure 4** MRI suggestive of an ill-defined lateral mass in the sphenoids with erosion of left sphenoid wall.

**Figure 5** H&E × 100 section showing broad aseptate hyphae of mucor invading a blood vessel.

**Figure 6** CT scan suggestive of soft tissue mass involving sphenoid and causing destruction of bony margins and extension into sella turcica.
was given. The patient was subsequently discharged on Itraconazole. Six months after the first presentation, the patient had significant improvement in headache and vision. The eyeball movement was possible in all the directions. MRI showed pneumatisation of all the sinuses except mucosal thickening in the sphenoids. Nasal endoscopy revealed a healthy sphenoid sinus. The patient is doing well till date.

Case IV

A 19-year-old female presented with headache for 1 month. She had no nasal or ophthalmological symptoms. Headache was localised to the vertex region and was continuous but non-radiating. On examination, there were no significant clinical findings in the nose or eyes. All cranial nerves were normal. CT scan showed an ill-defined mass in the sphenoid causing the destruction of the intersphenoidal septum. An endoscopic sphenoidectomy was done and the caseous material in the sphenoid was sent to histopathology, which was consistent with aspergillosis with mucosal invasion. Her headache resolved with surgery. Patient was given Itraconazole for 2 months and the patient is doing well till date, i.e. the follow-up of 7 months. She was not given amphotericin B because she had no eye symptoms.

Case V

A 77-year-old man presented with headache for 1 month and decreased vision in the left eye for 15 days. Headache was localised to the vertex region. On examination, the left eye had diminished vision (6/36). However, the pupillary reflexes were normal. Right eye had no vision for 10 years because of some complication of cataract surgery. CT scan was suggestive of a well-defined mass in the sphenoid with the erosion of left lateral sphenoidal wall. An endoscopic sphenoidectomy was done and the caseous material in the sphenoid was sent to histopathology, which was consistent with invasive mucormycosis. His vision improved to 6/12 after surgery. Postoperative amphotericin B was given till 1.5 g taking into consideration the renal functions. The patient was subsequently discharged on Itraconazole. The patient is doing well till date, i.e. 3 months of follow-up.

Discussion

Fulminant aspergillosis and mucormycosis of the paranasal sinuses represents an important cause of morbidity and mortality in patients whose host defenses have been altered by primary disease or immunosuppressive therapy. But the pattern of involvement by this fungus is changing. Reports are being published about invasive paranasal sinus aspergillosis and mucormycosis in an immunocompetent host. Rhinocerebral mucormycosis usually occurs in the clinical setting of diabetic acidosis. It is characterised by the presence of broad non-septate hyphae of phycomycetes in deep tissue stain.

In an immunocompetent host, invasive paranasal sinus aspergillosis manifests as an indolent but relentlessly progressive course. Our patients were neither immunocompromised nor had any nasal complaints, which are typical of fungal sinusitis. None of our patients had diabetes. Characteristically, the earliest lesion indicating involvement is crusting of the anterior end of the inferior turbinate or adjacent part of cartilaginous septum. The maxillary antrum is the most common paranasal site of Aspergillus infection and Aspergillus is the most common isolate in the paranasal sinus mycoses in north India. The presentation in our patients was atypical as they were immunocompetent and had no nasal symptoms. They had headache, diplopia, inability to move the eye, diminution of vision which is not the usual presentation in aspergillosis. However, mucor do presents with visual symptoms. The range of duration of headache was between 25 days and 2 months. The duration of visual symptoms was within 15 days. Loss of vision and diplopia were the main eye symptoms.

All these patients had isolated involvement of the sphenoid sinus, which is relatively rare. Headache was the most common presenting symptom in our patients as in other reports of isolated sphenoid sinus involvement with other diseases. The headache was deep seated and retro-orbital. This was because of the innervation of the sphenoid sinus, which is derived from both cranial nerves V1 and afferent fibres, via the sphenopalatine ganglion. Visual changes were the second most common complex symptom in sphenoid diseases. Patients frequently reported blurring of vision and loss of visual acuity ranging from mild to total blindness, ptosis and inability to move the eyeball. The loss of vision was because of the optic nerve involvement. The diplopia was secondary to sixth nerve palsy, which is one of the earliest signs of diseased sphenoid. Nasal symptoms are one of the common symptoms in sinonasal fungal sinusitis of sphenoid, but none of our patients had any nasal symptoms.

Endoscopic examination of the nasal cavities is of utmost importance. It was on nasal endoscopy only that we found purulent secretions in the sphenethmoidal
The debris was sent for KOH staining, fungal culture and histopathological examination. In fixed tissue, the *Aspergillus* was found to be of smaller size, septate, dichotomous branching and having 45° angle of branches as reported in various studies.\(^{13}\)

Radiological diagnosis played an important part in identifying the areas of involvement. In our patients, there was isolated involvement of sphenoid sinus with erosion of the surrounding structures. CT scan PNS showed the presence of areas of increased attenuation in the paranasal sinuses because of fungus.\(^{14}\) MRI scan of nose, paranasal sinuses and brain was undertaken to know involvement of intracranial regions. It was reported as decreased signal intensity on T1 and much decreased signal intensity on T2 weighted images. Our patients had similar radiological features. The differential diagnosis of fulminant aspergillosis of paranasal sinuses could be mucormycosis, lethal midline granuloma, allergic fungal sinusitis or malignancies of nose and paranasal sinuses.\(^{1, 6, 11}\) However, the clinico-radiological features are not specific to distinguish aspergillosis from other sino-orbital pathologies. Therefore, a confirmatory diagnosis is made on histopathology only. There are dilemmas in the treatment of sinonasal aspergillosis. Also the extent and approach of surgery is not well-defined. Some authors advocate endoscopic approach to sphenoid sinus\(^{15}\) while some have preferred external approach especially when orbits are involved.\(^{6}\)

We used endoscopic approach in all our patients. Endoscopic sphenoidotomy and macroscopic removal of the disease with a generous margin of healthy tissue ensuring ventilation of the sphenoid sinus was done. The role of postoperative amphotericin B after radical surgical debridement is well defined in mucormycosis. But in cases of invasive aspergillosis, there are controversies. Some authors have used only itraconazole,\(^{8}\) some have used only amphotericin B\(^{16}\) and some have used both these drugs postoperatively.\(^{8}\) We gave amphotericin B to each patient except case 4, keeping a strict watch on renal function tests. After amphotericin B dose of 2 g, patients were discharged on itraconazole 200 mg b.d. The therapeutic effect of this medicine was best once the surgical clearance of the disease had been done. In spite of the above measures, the disease may get disseminated to surrounding structures and spread intracranially to cause death of the patient as was found in two of our patients.

**Conclusions**

The changing pattern of involvement of sphenoid sinus by fulminant mycosis (both aspergillosis and mucormycosis) in immunocompetent subjects presents a greater challenge for otolaryngologist, ophthalmologist and neurosurgeons. They should always keep their minds open to this possibility, whenever they encounter a patient with headache, loss of vision, impairment of eyeball movements and ptosis. Nasal symptoms may be absolutely absent in such cases. The key to successful treatment includes a thorough workup of the patient, radiological examination (CT scan and MRI scan), endoscopic examination of nose and paranasal sinuses, endoscopic clearance of the disease and vigorous postoperative antifungal therapy. The fungus can involve only sphenoid sinus without involving any other paranasal sinus and therefore a high index of suspicion is necessary to pick up these lesions at an early stage. Endoscopic debridement of the sphenoid sinus is a safe and effective way for the disease clearance. Postoperatively amphotericin B and itraconazole should be given. Both renal and liver function should be monitored. A regular follow-up should be done, which includes nasal cleaning by douches and nasal endoscopy.

**References**