Isolated invasive fungal sphenoid sinusitis-induced extensive bone erosion and severe meningoencephalitis: diagnosis and multidisciplinary management

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SUMMARY

Invasive fungal sinusitis (IFS) is more common in immunosuppressed patients but can also occur in immunocompetent hosts. While the non-invasive type of fungal sinusitis has usually a good prognosis, IFS is a potentially lethal condition.

We report the case of a woman in her 60s presenting an isolated fungal infection by *Aspergillus fumigatus* of the right sphenoid sinus, causing extensive bone erosion of its walls and complicated by severe meningoencephalitis. She was healthy without any immunosuppressive conditions. Methods of diagnosis, multidisciplinary management, follow-up and outcomes are documented.

Early-stage diagnosis of sphenoid sinus pathologies is often delayed because patients are usually asymptomatic. IFS of the sphenoid is more aggressive than other paranasal sinus and carries significant mortality. Early diagnosis and aggressive and multidisciplinary treatment are crucial to reduce sequels and improve patient's survival.

BACKGROUND

Fungal infection of the paranasal sinus is generally classified into different types based on the histological features according to the diagnosis criteria of deShazo *et al*;[1 2] allergic, chronic non-invasive (fungus ball), chronic invasive, granulomatous invasive and acute fulminant invasive fungal infection. In addition to this classification, other types such as semi-invasive fungal infection[3] and saprophytic colonisation[4] have been also suggested in the literature.

The sphenoid sinus is surrounded by important structures such as the cavernous sinus, optic nerve, internal carotid artery, cranial nerves, pituitary gland and orbital apex. Thus, making sphenoid invasive fungal sinusitis (IFS) more aggressive and dangerous than on other paranasal sinuses.[5]

Differentiation between acute and chronic IFS depends on the speed of progression; according to Chakrabarti,[6] acute lasts <4 weeks in immunocompromised patients and chronic for >3 months.

We report a case of isolated sphenoid IFS in a healthy immunocompetent patient. The IFS induced an extensive bony erosion of the sinus walls, complicated by cerebrospinal fluid (CSF) leak and severe fungal meningoencephalitis. Clinical manifestations, radiological and histological findings, medicosurgical management, outcomes and follow-up are documented.

CASE PRESENTATION

A woman in her 60s was admitted to the emergency department for suspected epileptic seizures in the context of right-sided headache lasting for 5 days. She was in good general health, and her medical background showed neither immunosuppressive conditions nor previous sinus surgery. There was no history of sinusitis or any sphenoid sinus infection's disease in the past. No history of epilepsy, head trauma or intake of any medications or drugs. There was no fever.

She presented repetitive episodes of fixed gaze and decreased consciousness lasting 10–20 s. She reported visual hallucinations with complex geometrical forms and an oppressive feeling near the temporal or occipital lobe. Otherwise, her neurological exam was initially unremarkable. The EEG confirmed seizure originating from the right temporal lobe.

Radiological workup by CT angiography of the brain showed multiple zones of hypodense collections in the subdural space with mass effect on the cerebral parenchyma (figure 1A) and complete opacification of the right sphenoid sinus with central calcifications and extensive bony-wall erosion. No signs of intracranial hypertension. MRI of the brain showed encephalitis foci in the right parahippocampal, right midfrontal and left parietal region (figure 1B–E). 3-D CT reconstruction showed multiple zones of bony erosion of the right sphenoid sinus, the lateral wall in contact with internal carotid artery, posterior and superior walls in height of the right clivus and focal erosion at the floor of the optic nerve (figure 1F–G).

The patient was hospitalised in the neurology department, where an extensive workup showed neither systemic infection nor immunosuppression. A lumbar puncture was pathological and revealed a mild pleocytosis with lymphocytes predominance (leucocytes 6.3/x 10^9/L including 96% of lymphocytes, erythrocytes 355/µL, proteins 1130 mg/L and normal glucose value at 4.2 mmol/L). General bacteriological, anaerobic and fungus culture was negative.

Prompt surgical drainage of the right sphenoid sinus was performed via a transnasal endoscopic approach, using a 3-D navigation system.

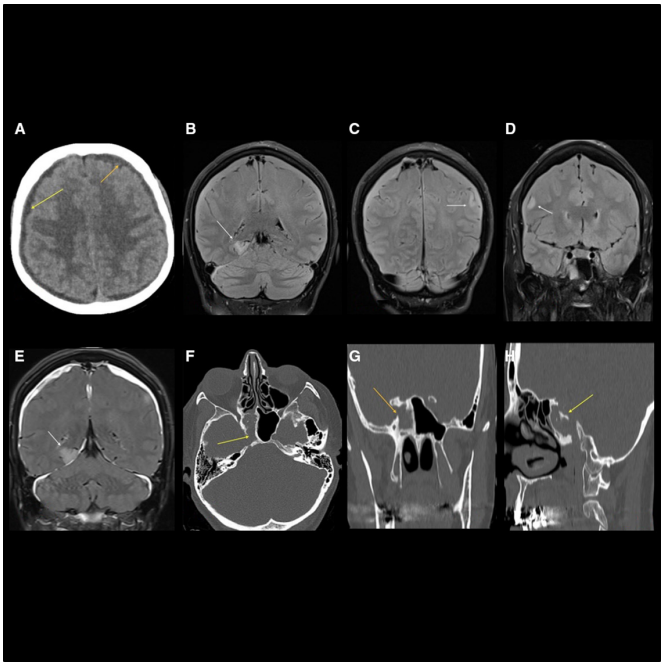

Figure 1 (A) Axial non-contrast CT soft tissues windowing shows multiple area of collection in the subdural space with mass effect. (B) T2 flair non-contrast coronal MRI shows foci of encephalitis in the right parahippocampal region. (C) T2 flair non-contrast coronal MRI shows foci of encephalitis in the left parietal region. (D) T2 flair non-contrast coronal MRI shows foci of encephalitis in the right mid-frontal region. (E) T2 with contrast coronal MRI shows foci of encephalitis in the right parahippocampal with aspect of reactional meningitis-contrast enhancement region. (F) Axial CT bony window shows total opacification of the right sphenoid sinus with large zone of bone erosion at the lateral sinus wall. (G) Coronal CT bony window shows extensive bone erosion at the lateral-posterior walls of the right sphenoid sinus. (H) Sagittal CT bony window shows large zone of bone erosion at the superior wall of the right sphenoid sinus.

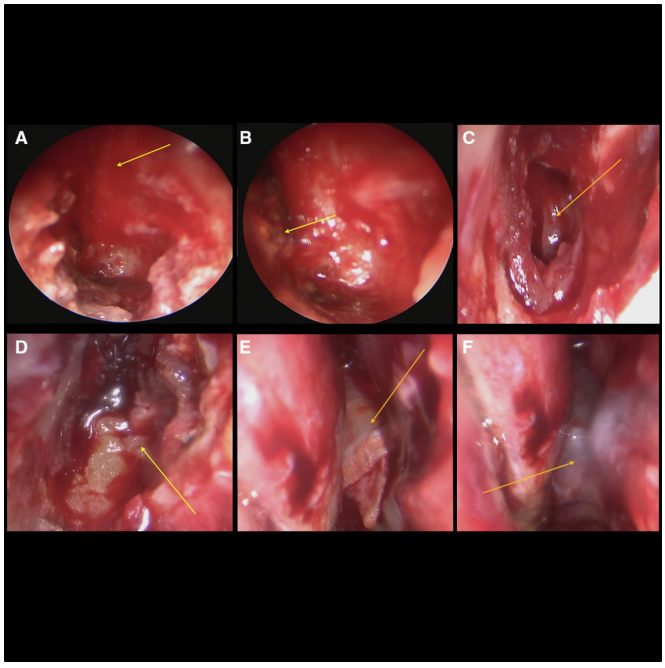

Figure 2 (A) Intraoperative endoscopic view after drainage of the right sphenoid sinus shows the extension of the bone erosion at the posterior wall. (B) Intraoperative endoscopic view after drainage of the right sphenoid sinus shows the extension of the bone erosion at the lateral wall. (C) Intraoperative endoscopic view of the revision surgery shows wide opening of the right sphenoid sinus with no recurrence of infection. (D) Intraoperative endoscopic view of the revision surgery shows plugging of the right sphenoid sinus with fat grafts. (E) Intraoperative endoscopic view of the revision surgery shows application of the fascia lata graft and fixation with adhesive tissues. (F) Intraoperative endoscopic view of the revision surgery shows total clopping of the right sphenoid sinus using different layers of grafts.

Nasal endoscopic evaluation during the surgery showed normal appearance of the nasal mucosa with no presence of purulent secretions or any other inflammatory signs in both nasal cavities. After complete drainage of the sinus, a large area of bone erosion at the lateral sinus wall was observed (figure 2A,B). The microbiological analysis by direct microscopic exam and after culture of samples taken from the contents of the sinus were positive for *Aspergillus fumigatus* and *Staphylococcus epidermidis*.

Multiple intravenous and oral treatments were administrated with antibiotics (Fortam, meropenem and clamoxycyline) and antifungal (amphotericin B and voriconazole). The antibiotic treatment was adapted according to the results of the antibiograms. Extensive bony erosion allowed for a sinus-meningeal communication with CSF leakage confirmed by B2-transferrin analysis. In order to protect the internal carotid artery, second sinus surgery was performed 2 weeks after the first sinus drainage. Fat grafts were harvested from the periumbilical area with fascia lata graft harvested from the right lateral thigh. The surgical procedure was performed by transnasal endoscopic approach, using the 3-D navigation system. The sphenoid sinus was plugged in three layers, and the grafts were fixed using adhesive tissues (figure 2C–F). The postoperative care was simple without complications.

During her hospital stay, the seizures became more complex with forced lateral gaze deviation to the left and right facial and arm twitching. She had several focal status epilepticus despite several antiepileptic drugs. Seizures were eventually controlled with levetiracetam, lacosamide, valproic acid and clobazam. The various EEG performed during hospitalisation showed a marked improvement. Different radiological evaluation by MRI and CT scan of the brain showed significant improvement of the encephalopathic foci and favourable aspect of the right sphenoid sinus.

The patient was discharged after hospitalisation of 49 days. The antifungal treatment by voriconazol was continued for an additional 6 months. Antiepileptic therapy by pregabaline 100 mg two times per day and levetiracetam 1 g two times per day was also continued.

Follow-up at 6 months showed absence of rhinology symptoms, nasal fibroendoscopy demonstrated good aspect and well integration of the grafts with complete sealing of the right sphenoid sinus. She experienced some focal autonomic and cognitive seizures during an attempt of antiepileptic drugs. She is currently seizure-free under three antiseizure drugs. After several months of rehabilitation, she was able go home and live with her husband. She is independent for daily activities but unable to work. She kept a mild anterograde memory impairment. She does not remember the first 3 months of her illness and suffers a degree of retrograde amnesia.

OUTCOME AND FOLLOW-UP

Surgical drainage of the right sphenoid sinus combined by medical treatment allowed to good local control of the fungal infections disease.

Plugging of the right sphenoid sinus was performed to protect the internal carotid artery and by using several types of graft.

Follow-up at 6 months showed free rhinology symptoms and good aspect of the right sphenoid sinus.

Neurology outcomes were favourable with regression of the meningoencephalitis.

Evolution of the epileptic seizures was favourable under several medication.

Neurology follow-up at 6 months showed free epileptic seizures, only minor sequel with mild anterograde memory impairment.

DISCUSSION

Isolated sphenoid sinusitis is rare and seen in fewer than 3% of all sinusitis. Patients with isolated fungal infection are rarer and considered as non-invasive, indolent form of fungal sinusitis.[7] Viral or bacterial infection of the sphenoid sinus can provide sufficient nutrients to the fungi, which start proliferating in a low pH medium, and sometimes forming a fungal ball.[8]

The clinical presentation of IFS of the sphenoid sinus is variable. Typical symptoms are prolonged diffuse headache and rhinorrhoea. Visual disturbance or ocular motion impairment results from orbital apex syndrome or cavernous sinus syndrome.[9] Headaches in sphenoid sinus lesions are deep seated and retro-orbital[10] but are a non-specific symptom, and its location do not suggest a sphenoid sinus disease.[11 12]

Due to the deep and posterior central location of the sphenoid sinus, rigid endoscopic examination of the sinus is difficult, and thus, flexible endoscopic examination is deemed more preferable. When IFS is suspected, early endoscopic evaluation with cultures of the sinus, contents and biopsy of the diseased tissues is strongly recommended.[13 14]

Sinus walls bony destruction on CT is a common finding on IFS, but extension beyond the sinuses may also occur with intact bone due to the fungi's ability to extend along the vessels.[15] In the early stage of IFS, opacification of the sphenoid sinus is the most common finding on CT. MRI is superior to CT in evaluating intraorbital and intracranial extension beyond the sphenoid sinus. Moreover, MRI is more sensitive in detecting early changes of acute fulminant IFS than CT,[16] and perisinus invasion on MRI was the most sensitive and specific parameter.

Despite improvements in radiological methods, current imaging studies are not sufficiently sensitive or specific, and vague symptoms of sphenoid lesions lead to delayed presentation. Dong *et al*[5] reported in a 12-case series with IFS of the sphenoid: time to presentation ranged from 1 week to 1 year. New diagnostic tests, such as serum *Aspergillus* galactomannan, and β-glucan can be useful as screening tests, especially in immunocompromised patients.

Management of IFS of the sphenoid should be adapted on each case. Often, early-aggressive sinus debridement and antifungal agents are the mainstays of treatment. However, important neurovascular structures adjacent to the sphenoid sinus may limit the extension of the surgery. Management of complications should be multidisciplinary and adapted to each situation. Regarding orbital complications, Dhiwakar *et al*[17] reported that orbital exenteration could be justified for posterior orbital (retrobulbar and apical) disease regardless of the functional status of the eye but is not recommended for anterior orbital (inferomedial) disease. However, orbital exenteration does not guarantee a cure of IFS.

Multiple antifungal class agents are used; amphotericin B is advantageous by its broad spectrum of activity against *Candida*, *Aspergillus*, *Cryptococcus*, *Fusarium*, Mucorales and endemic fungi.[18] In cases with renal impaired function, the lipid complex and liposomal form of amphotericin are alternative drugs used. Injection of amphotericin in the retrobulbar space has been used recently for orbital aspergillosis.[19] Therapy with hyperbaric oxygen has been sporadically used in IFS.[20]

Our unusual case shows a healthy and immunocompetent patient without a history of sinusitis, presenting with non-specific epileptic seizures as a main clinical symptom. The diagnosis of IFS of the sphenoid was made incidentally during the work-up for epileptic seizures, at an advanced stage with already intracranial complications and massive bone destruction of the sinus walls.

Our management was multidisciplinary, with immediate extensive surgical debridement of the sphenoid sinus, followed by medical treatment and appropriate neurology care. Regarding our strategy to cover the eroded bony walls, especially the lateral wall exposing the internal carotid artery (rupture risk), filling and plugging of the sinus were performed secondarily. To our knowledge, a similar strategy has yet to be described in the literature.

In the clinical series reported by Dong *et al*,[5] 6 out of 12 patients with sphenoid IFS had an extension into the intracranial region. Among these six patients, two developed subarachnoid haemorrhage due to aneurysmal rupture of the internal carotid artery.

In our case, the evolution was favourable with good control of the infection's disease and absence of severe squeals. Rhinology follow-up at 6 months showed absence of recurrence and good aspect of the right sphenoid sinus. Neurological follow-up is still ongoing.

Learning points

- Invasive fungal sinusitis (IFS) of the sphenoid sinus is rare but can be fatal.
- Early diagnosis of IFS of the sphenoid, aggressive and multidisciplinary treatment is crucial to reduce sequels and improve survival.
- Early-stage diagnosis of sphenoid sinus pathologies is often delayed because patients are usually asymptomatic and may present unspecific symptoms such as epilepsy.
- Sinus bony-wall erosion should not be underestimated—bleeding risk—and our original technique allows for an efficient and safe reconstruction.

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