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Unusual presentations of isolated sphenoid fungal sinusitis

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Abstract
Isolated sphenoid fungal sinusitis is a rare and often difficult to diagnose condition as the presenting symptoms are often vague and non-specific. In this series each case has a different clinical presentation with a different causative fungus. Although isolated fungal sphenoid sinusitis is usually seen in immunocompromised individuals, two of the three cases presented were immunocompetent. The fungi were *Pseudallescheria boydii, Aspergillus fumigatus* and *Schizophyllum commune*. In order to illustrate the great diversity of clinical signs, each case is individually presented. The characteristic radiological signs and the clinical management of each case are also presented. The danger signs of associated pathology are discussed with particular reference to an associated squamous carcinoma in one case. Surgical options and chemotherapy are discussed. Isolated sphenoid fungal sinusitis is a rare condition that if undiagnosed may result in considerable morbidity and even mortality of patients.

Key words: Sphenoid sinus; Infection; Fungi

Introduction

Isolated sphenoid sinus disease is a rare condition[1] with isolated fungal sinusitis making up a very small proportion of cases.[2] Consequently the clinical presentation and management of isolated fungal sphenoid sinusitis is largely undocumented, although it is thought to be similar to isolated bacterial sphenoid sinusitis. In these patients the disease is often missed as the most common presenting symptom is a central unresolving headache. It is rare for these patients to present with typical symptoms of sinusitis such as nasal obstruction, rhinorrhoea and post-nasal drip. Consequently in a large number of patients, the first time isolated sphenoid sinusitis is thought of is when the opaque sinus is seen during a computed tomography (CT) head done for investigation of unresolving headache. In a certain percentage of patients, cranial nerve palsies may be the presenting symptom. An isolated opacified sphenoid sinus on CT or magnetic resonance image (MRI) scanning will often be the only pathological finding. Isolated bacterial sphenoid sinusitis does not have a predisposition for occurring in immunocompromised patients while this is usually thought to be the case for isolated fungal sphenoid sinusitis. In this series of patients with isolated fungal sphenoid sinusitis, the symptoms, signs and associated pathology are presented and warning signs of possible concomitant disease elucidated. In addition the investigation and treatment of these patients is presented and options discussed.

Case reports

Case 1

A diabetic, 85-year-old woman who had had previous segmental mastectomy for breast carcinoma was referred with a six-month history of diplopia as her only symptom. She did not experience any headache, nasal or otological symptoms. On examination, the only abnormality was partial left IIIrd cranial nerve palsy with partial left ptosis and polyps in the spheno-ethmoidal recess. The serum eosinophil count was normal. The CT scan showed an extensive left sphenoid sinus mass with different densities and erosion of the petrous apex. There was also extension into the cavernous sinus and adjacent skull base (Figures 1 and 2).

An endoscopic sphenoidotomy and clearance of left spheno-ethmoidal recess polyps was performed. Extensive fungal debris (brown and green semi-solid inspissated secretions) with a cholesteatoma-like matrix was found in the sphenoid. The mucosa lining of the sphenoid was grossly inflamed and oedematous and very vascular. Tissues were sent for histological examination, microscopy, fungal culture and sensitivity.

On histology the cholesteatoma-like matrix was found to contain parakeratotic squames with nuclear atypia. Although no evidence of carcinoma was found on any of the specimens, the nuclear atypia was thought to be suspicious. The brown/green debris was septated branching fungal hyphae consistent with *Aspergillus* species. Invasive fungus was not seen and *Pseudallescheria boydii* (*P. boydii*) was cultured. The patient recovered well from the surgery and was discharged two days later. A nasoendoscopy two weeks later revealed healthy sphenoid sinus mucosa without evidence of residual disease. The patient was from the country and failed to attend further follow-up. When she eventually returned she had complete resolution of her IIIrd cranial nerve palsy. However, she was noted to have developed a partial VIIth nerve palsy that gradually became complete. A repeat CT scan showed an opacified left sphenoid sinus with largely unchanged destruction of the petrous apex. The sphenoid sinus was re-explored endoscopically and a small amount of fungal

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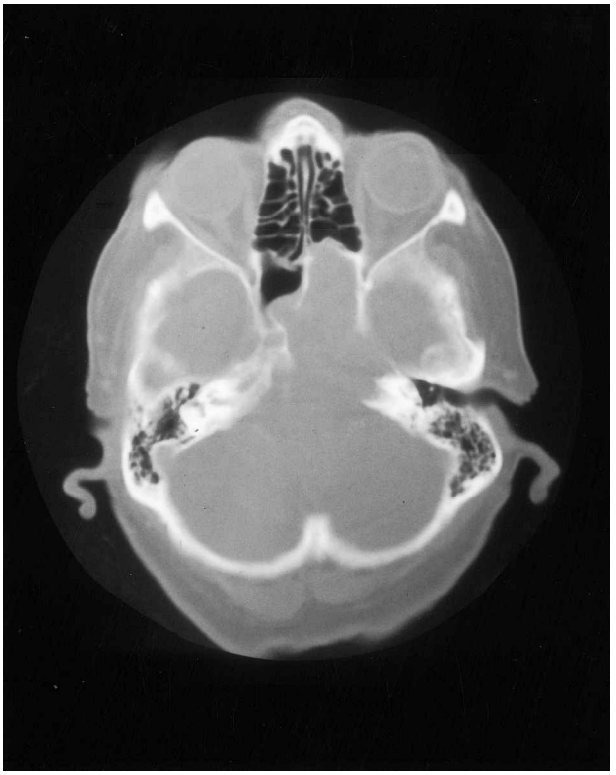

FIG. 1

CT scan of the patient (*Case 1*) who presented with left-sided partial IIIrd cranial nerve palsy and partial ptosis demonstrates extensive left sphenoid sinus opacification and petrous apex erosion.

debris was found with a large amount of cholesteatoma-type matrix. On this occasion histology showed invasive poorly differentiated squamous cell carcinoma. Post-operatively, her condition continued to deteriorate and the patient eventually died.

Case 2

A 60-year-old Caucasian woman presented in June 1995 with left-sided nasal obstruction secondary to left-sided maxillary fungal sinusitis with a macroscopic appearance resembling *Aspergillus* sp. She underwent left intranasal ethmoidectomy, middle meatal antrostomy, inferior meatal antrostomy and clearance of fungal ball from the left maxillary antrum. Her sphenoid was clear at the time. Fungal elements were seen on microscopy. However, it failed to grow on fungal culture. She remained asymptomatic for about two and a half years. In November 1997, she presented with a six-week history of left-sided nasal obstruction, thick green rhinorrhoea, post-nasal drip, epistaxis and left side retro-orbital pain. On endoscopy she had polyps in her spheno-ethmoidal recess. Repeat CT scan (Figure 3) showed an isolate opacified left sphenoid sinus (previously clear). She underwent left intranasal polypectomy and sphenoidotomy. Polyps and thick waxy brown debris in left sphenoid sinus was removed. Fungal culture grew *Aspergillus fumigatus*. Two weeks after surgery, the sphenoid sinus was clear and the sphenoid ostium was patent. The patient has been followed up for six months without recurrence of disease.

Case 3

A 37-year-old immunocompetent female was admitted with a two-day history of recalcitrant headache and neck pain for investigation. She had a past history of recurrent

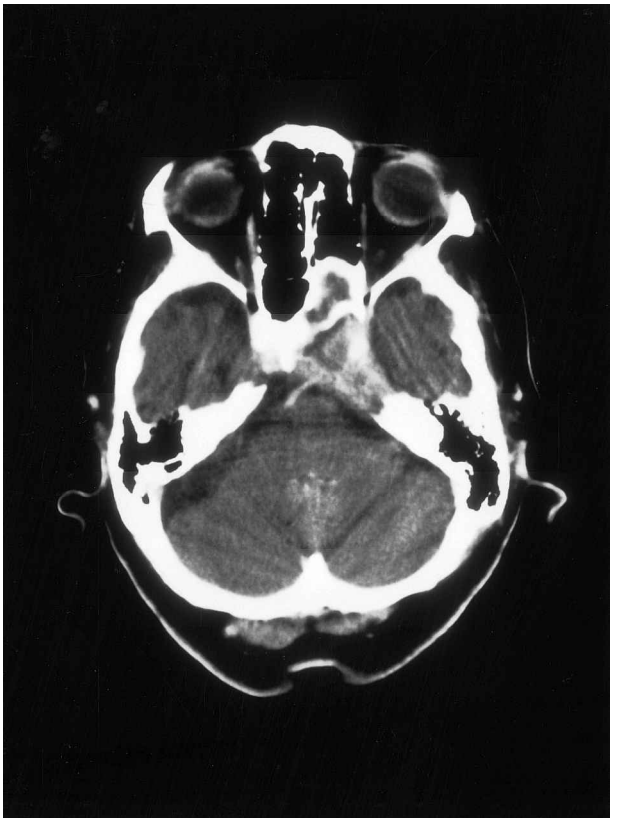

FIG. 2

CT scan of the patient (*Case 1*) on soft tissue setting demonstrating double densities in sphenoid sinus compatible with the diagnosis of fungal sinusitis.

migraines, hayfever and asthma. She was also a keen swimmer. She presented with severe constant bifrontal headache radiating to the occiput. It was similar to her previous migraine pain but more severe in nature. There were associated symptoms of nausea, vomiting, photo-

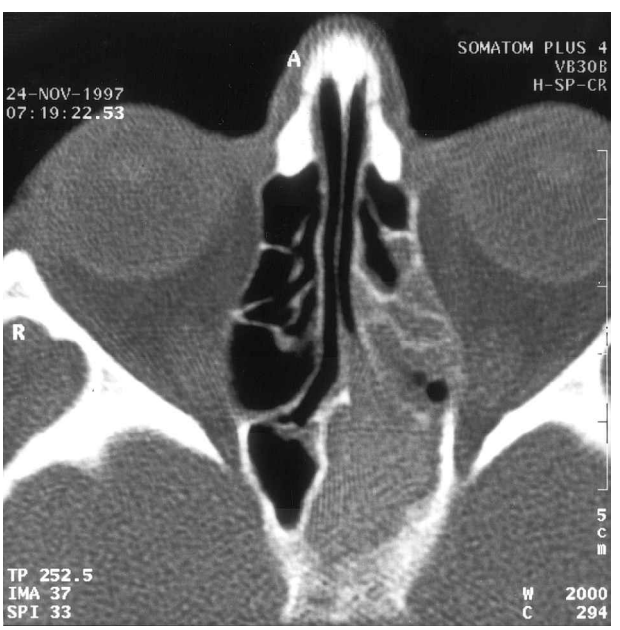

FIG. 3

CT scan of the patient (*Case 2*) with *Aspergillus fumigatus* sinusitis demonstrates opacified left sphenoid sinus and adjacent posterior ethmoids.

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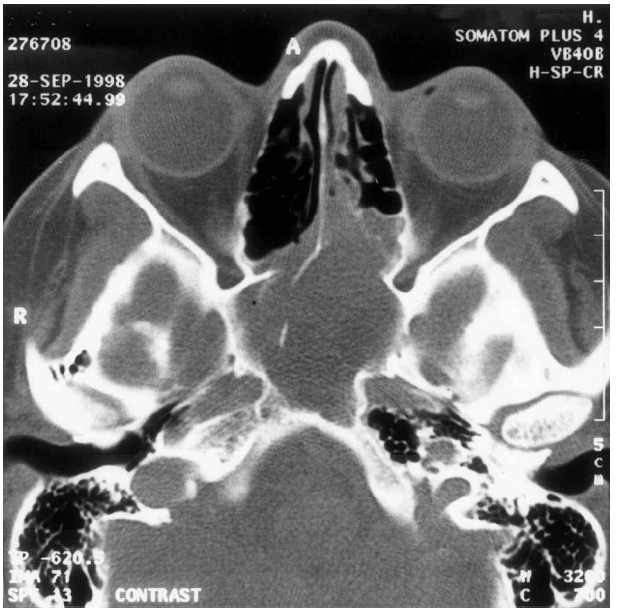

FIG. 4

CT scan of the patient (*Case 3*) with *Schizophyllum commune* sinusitis shows a complete opacification of the left sphenoid sinus with erosion of the anterior wall.

phobia and rhinorrhoea. Clinically she was afebrile and there was no focal neurological sign or neck stiffness.

The CT scan revealed a complete opacification of the left sphenoid sinus with erosion of the anterior wall (Figure 4). Although a diagnosis of headache secondary to sinusitis was made, the patient was not referred to an otolaryngologist and discharged on amoxycillin. The patient represented with worsening pain and rhinorrhoea. On review by an otolaryngologist, a watery red eye with intra-nasal pus was noted with a partial left VIth nerve palsy. The patient was afebrile. Ocular examination and other cranial nerves were otherwise normal. A repeat CT scan was done to exclude extension of the sphenoid disease. A marked increase of eosinophil count (2.36×10^9/L) was noted. At surgery two nasal polyps were noted in the sphenoethmoidal recess and on sphenoidotomy a fungal ball was found adherent to the lateral wall overlying the optic canal. Microscopy and culture showed fungal hyphae with a staphylococcal coagulase-negative species and the fungus was identified as *Schizophyllum commune*. This was sensitive to amphotericin and itraconazole but was resistant to fluconazole. On immunodeficiency screen the chest X-ray, HIV/hepatitis serology, immunoglobulin levels (not IgE) and complement levels were normal. The patient was commenced on a course of amphotericin B for two weeks and then given an eight-week course of itraconazole. Ten days later her headache and diplopia had resolved. A repeat CT scan was done to exclude any residual disease. This showed mucosal thickening but was otherwise clear.

Discussion

Isolated sphenoid sinus disease is very rare with Hnatuk *et al.*[3] in 1994 reporting only 63 cases in the medical literature since 1934. Isolated fungal disease of the sphenoid sinus is even rarer with only a few cases having been reported in the literature.[4] It is interesting to note that most of the cases of isolated fungal disease of the sinuses has been associated with hot dry climates such as Sudan, Northern India and Saudi Arabia. Southern Australia (where this series occurred) also experiences hot and dry conditions during the summer months. It is still unclear, however, whether this is a result of the dry climate causing impairment of the local defence systems or if the fungal spore counts are significantly higher in these regions.[5] Isolated fungal sinusitis is most often associated with immunocompromised patients particularly diabetic patients and patients on long-term steroids.[4] While *Aspergillus fumigatus* is the most commonly involved fungus,[6] both *Schizophyllum commune* (*S. commune*) and *P. boydii* infections have been reported.[7–9] Isolated sphenoid sinusitis including isolated fungal infections of the sphenoid may have a very indolent course with few clinical signs and surgeons often rely on radiology for diagnosis. As the diagnosis is often delayed, the vital structures in and around the sphenoid may become affected and patients will often present with bizarre neurological complications as the first manifestation of their disease.[10] In this series, *Case 1* presented with an isolated partial IIIrd nerve palsy while *Case 3* presented with an isolated VIth nerve palsy. Headache and retro-orbital pain may also be prominent features as in *Case 2*. *Case 1* also illustrates the need for the treating surgeon to be aware of the possibility of concomitant pathology. In this case the first biopsies revealed squamous cell atypia in association with the fungal infection. However, repeat biopsies revealed the underlying squamous carcinoma in association with the fungal infection. Although the fungal ball filled the sphenoid sinus, it is likely that its growth was secondary to that of the squamous carcinoma. Bony destruction is common both for *Aspergillus* infections as well as for carcinoma and this should be kept in mind during the follow-up care of isolated fungal sinusitis patients. Other tumours may also primilary involve the sphenoid sinus. These include pituitary tumours, craniopharyngiomas, meningiomas and other tumours including metastatic tumours.[1] These need to be considered and excluded during the initial management of the patient.

The primary treatment consists of surgically opening the sphenoid sinus. This is best achieved under endoscopic control and with angled telescopes for this allows complete removal of all fungal material from the sphenoid sinus.[11] Removal of the superior turbinate with creation of a large opening into the sphenoid should allow post-operative endoscopic visualization of the sphenoid.[11] This should allow early detection of any recurrence of disease. Further medical treatment of the fungus will depend upon whether the fungus was invasive or not. Both *Aspergillus* and the *Pseudallescheria* species may be invasive with bony destruction and histological evidence of tissue or vascular invasion. However, *P. boydii* infection is rarely invasive in human, and most infection in humans is in the form of fungal ball or mycetoma.[5] Adequate treatment of *P. boydii* infection can be achieved with surgical debridement and adequate aeration of the sinus.[5]

In *Case 1* antifungal agent was not beneficial as the primary pathology was the invasive squamous cell carcinoma. In *Case 2* an immunocompetent patient presented with non-invasive *Aspergillus* sinusitis without bony destruction or cranial nerve involvement. Surgical debridement alone is usually adequate for non-invasive *Aspergillus* sinusitis.[5] Antifungal agents were given to the patient in *Case 3* because of the rapid progression of the disease with cranial nerve involvement. If adjuvant antifungal agent is indicated, the drug regime should be determined by culture and sensitivity as microscopy may not always be able to differentiate between the fungal species. In *Case 1* the histological examination of fungus showed features suggestive of *Aspergillus* sp., however, subsequent culture showed the fungus to be *P. boydii*. It is morphologically impossible to distinguish hyphae of *P.*

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boydii from those of *Aspergillus* sp. as both have septate, branching hyphae.[7,12,13] The accurate identification of *P. boydii* is of paramount importance since *P. boydii*, unlike *Aspergillus* and *Schizophyllum*, is uniformly resistant to amphotericin B.[7,12] While the first line antifungal therapy for invasive fungal infections of the sinuses remains Amphotericin B, this may need to be changed to the azoles.[7] Miconazole has been shown to be a well-tolerated and highly effective agent for the treatment of *P. boydii* infection.[7,12]

This series of isolated sphenoid sinus fungal sinusitis illustrates the bizarre presentation and varied pathology that is associated with this disease. A high index of suspicion is necessary in both the diagnosis and ongoing management of these patients. Endoscopic surgery with adjuvant chemotherapy remains the mainstay of treatment for the disease.

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