

Isolated sphenoid sinus aspergillomas*

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ABSTRACT

Fungi are more often than previously believed to be the causative organisms of paranasal sinusitis. Aspergillus, a fungus belonging to the Ascomycetes class, accounts for the majority of these infections, which affect not only debilitated patients but healthy people as well. There are two distinct clinical forms of Aspergillus sinusitis, invasive and non-invasive, and each of them is further divided in two subtypes. Isolated aspergillosis of the sphenoid sinus is a rare disease, which is usually misdiagnosed for a long time because of its varying symptomatology. In the present study, four cases of isolated sphenoid Aspergillus disease are described and the recent literature is reviewed. Physicians should be aware of this rare clinical entity, as in many cases early diagnosis and appropriate treatment provide the key to achieve favourable outcomes.

Key words: sphenoid sinus, sphenoiditis, aspergillosis

INTRODUCTION

Fungal sinusitis is a well-recognised clinical entity, most often affecting the maxillary sinus (Miglets et al., 1978; Romett and Newman, 1982; Koop et al., 1985; Blitzer and Lawson, 1993). During the last decade many cases of fungal sinusitis have been reported at an increasing rate. This fact may be partially due to an improvement in diagnostic methods. Nevertheless, an absolute increase in patients suffering from fungal sinusitis may have occurred as well.

Aspergillus fumigatus is considered to be the most common fungus isolated from the paranasal sinuses (Stammler et al., 1984; White, 1991; Brandwein, 1993). However, the array of fungi which have been reported as the causative organisms is broad (Washburn et al., 1988). Most of them are saprophytic in the oral and nasal cavities (Washburn et al., 1988; White, 1991; Hartwicz and Batsakis, 1991).

The key to early diagnosis of paranasal fungal disease is a high index of suspicion. Computed tomography (CT) and magnetic resonance imaging (MRI) are extremely helpful in identifying and classifying the disease and choosing the appropriate treatment (Washburn et al., 1988; Som, 1993; Roithmann et al., 1995).

Although it happens rarely, the sphenoid sinus can also be invaded by fungi, either alone or in combination with other sinuses (Miglets et al., 1978; Lavelle 1988). The close relation between the sphenoid sinus and important anatomical structures (such as the internal carotid artery, cavernous sinuses, optic nerve, et cetera) makes early diagnosis and management imperative. In the present paper, we report four cases of isolated sphenoid

aspergillosis, which were identified and treated in our department during the last year. The recent literature is also reviewed.

PATIENTS AND METHODS

Between October 1995 and February 1996, four female inhabitants of Athens were diagnosed and treated for isolated sphenoid fungal disease at our department. None of these patients was immunocompromised nor received long-term corticosteroids. One of them (case 3) was presented on admission with a recently installed unilateral hearing loss and a pre-existing (since two years) headache. Case histories obtained from the patients and clinical examinations did not pinpoint the site of the lesion, but imaging studies did so. All patients had positive findings for non-invasive isolated sphenoid disease on CT scans (Figure 1A). Two patients (cases 3 and 4) also had magnetic resonance images which were consistent with fungal sphenoid disease as well. (Table 1 summarises the pre-operative clinical and radiological findings of the patients.)

Endoscopic sphenoidotomy of the involved sinus with anterior sinus wall removal was applied in all patients, under general anaesthesia. Thus, adequate drainage was ensured. The material found in the sinuses was removed. The mucous membrane in all cases was slightly thickened, so the sinus mucosa was left intact, avoiding a possible iatrogenic injury to the surrounding fine structures, however, biopsies of the mucosa were obtained in all cases.

The diagnosis was based on the CT scan and operative findings and was definitively confirmed by histological studies.

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Table 1. Patients' pre-operative findings.

case	age/sex	main symptoms	duration of symptoms	other	CT-scan findings
1	45 F	headache	3 years	middle anemia (Ht 34%)	left sphenoid occupied
2	43 F	headache	14 months	deviated septum	left sphenoid
3	55 F	headache, postnasal drip	2 years	unilateral hearing loss, hypertension, hypercholesterinemia	left sphenoid
4	77 F	headache	20 months	hypertension, nephrolithiasis	right sphenoid

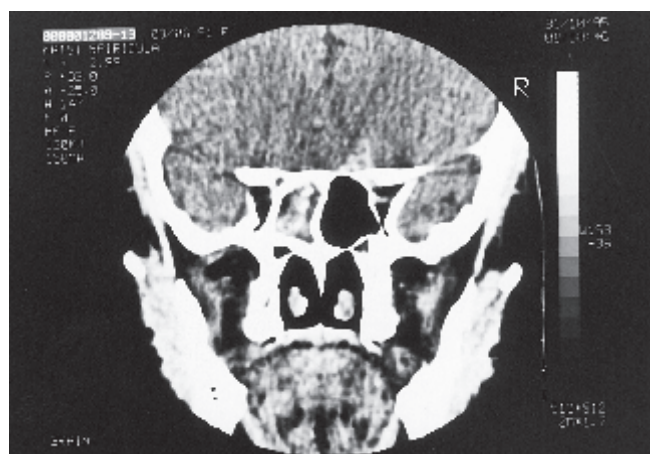


Figure 1A. Case 1: coronal CT-scan revealing complete opacification of the left sphenoid sinus. Extremely dense particles are also observed within the fungal mass.

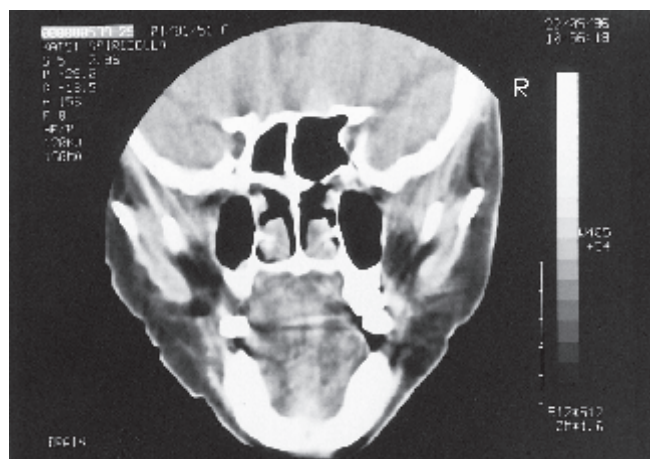


Figure 1B. Case 1: post-operative CT findings.

RESULTS

Immediate relief of the patients' complaints was achieved in all cases (Figure 1B). A rare, intermittent headache continued only in patient 4.

Histological examination of the cheesy masses removed from the sinuses demonstrated entangled septate hyphae of *Aspergillus*, showing dichotomous branching at an angle of 45°. The sinus mucosa was found to be intact, without fungal invasion. Cultures obtained from sphenoid sinus fluids were not always consistent with the final diagnosis.

Table 2. Treatment applied, micro-organism revealed and follow-up results of each patient.

case	treatment	organism	hospitalisation days	follow-up/recurrence
1	surgery	<i>Aspergillus</i>	6	10 months, no recurrence
2	surgery+ antifungal	<i>Aspergillus</i>	5	8 months, no recurrence
3	surgery+ antifungal	<i>Aspergillus</i>	4	7 months, no recurrence
4	surgery	<i>Aspergillus</i>	4	6 months, no recurrence

Table 2 describes the treatment applied to each patient, the organism revealed by histological examination and the follow-up period in each case.

On the basis of CT scans, operative and histological findings (Figures 2A-B), the above-mentioned cases were all characterized as isolated sphenoid mycetomas (aspergillomas).

In cases 2 and 3, because of the thin anterior sphenoid wall observed during operation, a semi-invasive or chronic invasive aspergillosis was initially suspected and an intra-oral course of itraconazole (200 mg once daily, for one month) was administered post-operatively. No recurrence of the disease has been observed so far, either clinically or on CT scans.

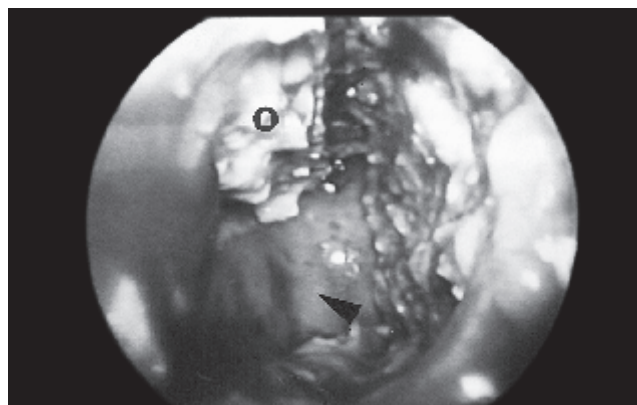


Figure 2A. Case 4: endoscopic appearance of the sinus at the time of surgery (the arrowhead indicates indentation of right internal carotid artery, the circle denotes the fungal mass).

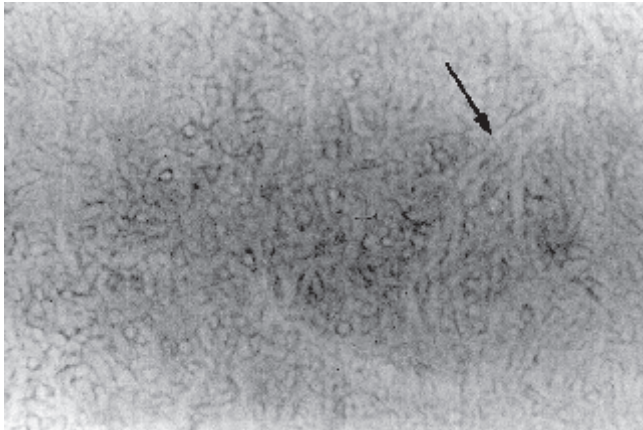


Figure 2B. Histological view of septate hyphae and dichotomous branching (arrow), an indication of *Aspergillus* sinusitis, confirmed the diagnosis (haematoxylin and eosin stain; ×400).

DISCUSSION

Fungal disease of the nose and paranasal sinuses is not a common problem, however, in the recent literature, fungal sinusitis has been reported with increasing frequency. *Aspergillus* species are by far the most common invaders of the paranasal sinuses and the maxillary antrum represents the site most commonly infected.

Table 3. Classification of fungal sinusitis (based upon information provided in Hartwicz and Batsakis [1991], White [1991], Blitzer and Lawson [1993], Brandwein [1993], and Saeed and Brookes [1995]).

1. invasive or mucosal (or penetrating) form:
a) <i>chronic</i> or indolent
b) <i>fulminant</i> or acute
2. non-invasive or extramucosal form:
a) <i>mycetoma</i> or aspergilloma
b) <i>allergic fungal sinusitis</i>

Two main categories of fungal sinusitis are presently recognised (Table 3): *invasive* and *non-invasive* (Hartwicz and Batsakis, 1991; White, 1991; Brandwein, 1993; Blitzer and Lawson, 1993; Saeed and Brookes, 1995). The invasive form, also called mucosal or penetrating sinusitis, is further classified into two subtypes, the *chronic* (or: indolent) and the acute (or: *fulminant*) fungal sinu-

itis. The latter is mainly found in immunocompromised neutropenic individuals and requires rapid diagnosis and aggressive treatment, representing a medical emergency (White, 1991). In contrast, the non-invasive or extramucosal form is benign in nature, and also consists of two distinct subtypes: the *mycetoma* and *allergic fungal sinusitis*, previously mentioned as allergic *Aspergillus* sinusitis (Katzenstein et al., 1983; Ronson et al., 1989). Except for the fulminant variant, the other types are encountered in apparently healthy individuals (Zinneman 1972; Pearlman et al., 1989; Blitzer and Lawson, 1993). In Table 4, the main characteristics of the four subtypes of fungal sinusitis are reviewed (Waxman et al., 1987; Hartwicz and Batsakis, 1991; Blitzer and Lawson, 1993; Saeed and Brookes 1995).

Isolated sphenoid fungal disease is rare, and when it occurs misdiagnosis is the rule, since isolated sphenoid sinusitis usually presents as a headache of unknown aetiology – tantalising the patient for months or even years – or may mimic an intracranial process. The relationship of the sphenoid sinus to important adjacent structures accounts for the neurological symptoms and signs observed in the cases of sphenoid infection (Proetz, 1948; Wyllie et al., 1973; Kron and Johnson, 1983).

Diagnosis is confirmed by surgery and histopathology, the latter revealing characteristic septate branching hyphae. Differential diagnosis should include bacterial infections, granulomatous inflammations and, generally, all sorts of sinus occupying masses – such as polyps, mucocele and pyocele, aneurysms, primary sphenoid tumours (e.g., squamous cell carcinoma), secondary sphenoid invaders (craniopharyngioma, nasopharyngeal angiofibroma, et cetera) and metastatic tumours (Wyllie et al., 1973; Washburn et al., 1988; Knwon-Chung and Bennett, 1992). The prominent symptom relevant to the sinus disease of all our patients was a long lasting headache. The pain was mainly localised in the retro-orbital (cases 1 and 3), frontal (case 4) and temporo-parietal areas (case 2). Its duration varied from 15 months to 3 years with periods of remission. All patients had received multiple courses of antibiotics with concomitant analgesic abuse without satisfactory results.

It is commonly accepted that prolonged antibiotic therapy – for any reason – may alter the normal flora of the sinuses, predisposing to fungal growth (Bahadur et al., 1983; Romagnoli, 1993;

Table 4. The most important features of the fungal sinusitis are summarized (based upon information provided in Hartwicz and Batsakis [1991], White [1991], Blitzer and Lawson [1993], and Saeed and Brookes [1995]).

type of sinusitis	host's status	sinus involved	tissue invasion	treatment	prognosis
mycetoma (aspergilloma)	healthy	maxillary sinus (as usual)	none	sinus debridement, aeration	good
allergic <i>Aspergillus</i> sinusitis	atopic	multiple sinuses	none	sinus debridement, aeration, steroids	good
chronic invasive	healthy	multiple sinuses	yes	surgical extirpation, antifungal agents	variable
fulminant	immuno-compromised	multiple sinuses	yes	urgent surgical extirpation, antifungal agents	poor (high mortality)

Blitzer and Lawson, 1993). Therefore, in some cases, the participation of antibiotic agents in the pathogenesis of fungal infections cannot be excluded.

As we have already mentioned, the main symptom – headache – completely subsided in all cases but one (case 4). We believe that the rare bouts of headache observed post-operatively in the latter case were irrelevant to the sinus disease, the patient showing a neurotic character. However, one should be very cautious in attributing any persistent headache to psychological disorders, especially in the post-operative patient.

None of our patients complained of any visual or other neurological symptoms, thus proving the non-invasive nature of aspergillomas. Likewise, bone invasion was not observed on CT scans in any of our patients; on the contrary, extremely dense areas deep inside the fungal masses were identified in all cases. This finding is considered pathognomonic for aspergillosis of the paranasal sinuses and is due to calcium phosphate and, to a lesser degree, calcium sulphate accumulation in necrotic areas, towards the center of the fungal mass (Stammberger et al., 1984; Saeed and Brookes, 1995).

It is noteworthy that all our patients were female, three of them were middle-aged while case 4 was an elderly woman. A slight deviation of the nasal septum towards the site of the lesion was observed in case 2; however, in the rest of the patients none of the well-accepted predisposing factors – such as the taking of steroids or cytotoxic drugs, diabetes, allergy, immunological deficiencies, maxillofacial trauma or anatomical irregularities of the facial skeleton (Miglets et al., 1978; Holt et al., 1984) – was recognised.

Intra-operatively, a thin anterior sphenoid wall was identified in cases 2 and 3. This finding casts doubt on the non-invasive nature of the disease; however, mucosal invasions have not been confirmed histologically.

Although the follow-up period is too limited for drawing definitive conclusions, all four patients are symptom-free up to now, despite the contrary reports in the recent literature (Washburn et al., 1988; Knwon-Chung and Bennett, 1992; Blitzer and Lawson, 1993). Based on our results, we suggest that endoscopic sphenoidotomy and the establishment of adequate sinus drainage are sufficient in order to treat non invasive sphenoid aspergillomas. Systemic antifungal agents are recommended when there are signs of invasion, i.e., mucosal involvement or extension to posterior ethmoidal cells.

Isolated sphenoid sinus aspergillosis, although rare, is accompanied by increased morbidity or even mortality in the case of invasive disease. In accordance with Wyllie et al. (1973), we believe that awareness, suspicion, detailed examination, aggressive intervention and long-term follow-up are the key to successful treatment.

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