

Paranasal sinus mycosis in suspected fungal sinusitis

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ABSTRACT

Background: Fungal infections of the paranasal sinuses in the immunocompetent patients are being recognized with increasing frequency. Infections are assigned in invasive and noninvasive forms.

Materials and methods: In a retrospective study, a total 39 patients with suspected fungal sinusitis were studied for causative fungal agents between 1994 and 2001. Diagnosis was confirmed by demonstration of fungi in direct preparations and culture techniques. Samples were biopsy specimens taken from the sinuses or exudates from deep sinus tracts.

Results: Paranasal sinuses mycoses were proven in 18 patients, including 12 men and 6 women, their age ranging from 17 to 58 years. The most frequently isolated organisms were *Aspergillus* spp. and *Candida* spp. Paranasal sinuses infections by *Cladosporium trichoides* (bantuanum) and *Pseudallescheria boydii* are reported for the first time in Iran from Pasteur Institute.

Conclusion: In our series, *Aspergillus flavus* has been isolated more frequently than other agents.

Keywords: *Fungal infection, Paranasal sinuses infection, Sinuses mycoses.*

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INTRODUCTION

Although fungal infections of the paranasal sinus are uncommon, 3-5% of cultured sinus samples are positive for fungi (1). *Candida* and *Aspergillus* species are more frequently found, however, less commonly zygomycete or other mould fungi are cultured (2).

DeShazo and colleagues have proposed new classification for invasive and noninvasive fungal sinusitis (3). They explained three forms of invasive fungal sinusitis and proposed the terms: granulomatous, acute fulminant, and chronic

invasive, which can also be seen in immunocompetent patients. On the other hand, the noninvasive fungal sinusitis have been classified as allergic fungal sinusitis (AFS) and fungus ball (3). Invasiveness is determined by tissue histology of mucosal invasion. Stringer and Ryan described chronic invasive fungal sinusitis as an entity usually occurring in healthy individuals who have chronic sinusitis symptoms, bone erosion on computed tomography (CT) scan, and involvement of adjacent structures (orbit, cribriform plate, etc) (4).

Histopathologic findings of granulomatous and nongranulomatous chronic invasive fungal sinusitis show the presence of the hyphal fragments within

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the tissue. The granulomatous type shows granulomas composed of eosinophilic material surrounded by fungi, giant cells, and palisading nuclei. The nongranulomatous type is characterized by tissue necrosis with little inflammatory infiltrate and dense hyphal accumulation resembling a fungus ball. The fungi in this form may breach mucosal barriers to invade blood vessels or cause arteritis with no vascular invasion. Both granulomatous and nongranulomatous forms may result in tissue necrosis.

Paranasal sinus mycoses are common in north India, northern Sudan and south-western states of the USA. *Aspergillus flavus* is the most common agent isolated from affected patients (5,6).

For effective management, surgical debridement and sinus ventilation are recommended for non invasive situations, whereas the possible requirement of adjuvant medical therapy has been emphasized for the semi-invasive (non-invasive disease with bone destruction) and the invasive types to prevent recurrence and further extension (6,7). The highest mortality rate (33.3%) was reported among patients with zygomycotic infection (8).

Aspergillosis is by far the most common type of fungal disease affecting the paranasal sinus, where a number of different clinical syndromes have been associated with the presence of *Aspergillus* species (Table 1). Meanwhile, other mould fungi (*Fusarium* spp., *Curvularia* Spp., *Pseudallescheria boydii* and *Alternaria* spp.) could also be isolated from cases of sinusitis (2).

Table 1. Classification of paranasal sinus *Aspergillosis*

Colonization by <i>Aspergillus</i>
<i>Aspergilloma</i> of the paranasal sinuses
Allergic <i>Aspergillus</i> sinusitis
Invasive <i>Aspergillus</i> sinusitis
Acute invasive <i>Aspergillus</i> sinusitis
Chronic necrotizing <i>Aspergillus</i> sinusitis
Paranasal <i>Aspergillus</i> granuloma

PATIENTS and METHODS

Between 1994 and 2001, a total of 39 patients with suspected fungal infections of the paranasal sinuses were examined in the Medical Mycology Department, Pasteur Institute of Iran. Biopsy specimen or sinus washings were used for this purpose. Diagnosis was made by direct examination and culture. Direct preparations with the use of 10% KOH and dimethyl sulphoxide (DMSO) were made and specimens were cultured on SDA (sabouraud dextrose agar), sabouraud dextrose agar with chloramphenicol (50mg/ml), blood agar, brain heart infusion agar (B.B.L) and thioglycolate media.

Duplicate cultures on each medium were incubated at 35°C and 25°C regularly, examined up to 3 weeks and identified using standard methods. Microscopic features of the isolates were studied by slide culture preparation. The preparations were stained using Gram's technique in order to diagnose yeasts. Identification was based on biochemical properties, the ability to produce chlamydospores and the filamentation test.

For cultured mould fungi (*Aspergillus*, *Pseudallescheria boydii*), positive results of mycological examinations were accepted only if the direct examination was positive and if two successive culture growths of the same fungus specimen were observed. Cases which did not meet these criteria were regarded as negative and were not included in our study.

RESULTS

We have examined 39 samples for fungal infections of the paranasal sinuses. Fungi were isolated in 12 males and 6 females, their age ranging from 17 to 58 years (mean of 33.4 years).

There was one or more predisposing factors or associated conditions for fungal infections in 50% of the affected subjects (table 2). Table 3 outlines the isolated fungi of the paranasal sinuses.

Table 2. Predisposing factors or associated conditions to fungal sinusitis

Renal transplant recipient
Bone marrow neoplasm
Broad spectrum antibiotic therapy
Immunosuppressive chemotherapy
Chronic granulomatous disease (CGD)
Wegner's granulomatosis
Anemia
Asthma

Table 3. Isolated fungi from paranasal sinuses

Organism	Number(%)
Aspergillus flavus	5(27.8)
Aspergillus niger	1(5.5)
Aspergillus fumigatus	1(5.5)
Candida albicans	3(16.7)
Candida spp.	2(11.1)
Cladosporium trichoides (bantianum)	1(5.5)
Pseudallescheria boydii	1(5.5)
Actinomyces spp.	4(22.2)
Total	18(100)

For the first time in Iran, fungal sinusitis due to *Cladosporium trichoides* (bantianum) and *Pseudallescheria boydii* have been reported from Pasteur Institute (9). The case of the *Cladosporium trichoides* (bantianum) was an 18-year old male worker with Wegener disease. He had a long history of nasal obstruction and chronic sinusitis, headache, lacrimation, nasal congestion, nasal discharge, high fever, cough, hemoptysis, a mass in his left hemithorax and a black perforated necrotic lesion in hard palate measured 2.5×6.5 centimeters. His problem began when he was 16 years old with lacrimation, for which dacryocystorhinostomy was performed. Later on, CT of the paranasal sinuses showed an inflammation in maxillary sinus and an erosion spread to the right nasal cavity and hard palate. The diagnosis was established by histopathological appearance, direct examination, culture and computerized tomography (CT) scan. This case was successfully treated by a combination of surgery and amphotericin B

(1mg/kg/day). Oronasal perforation was also repaired by reconstructive closure.

The case of *P. boydii* was a 48-year old woman presenting with chronic sinusitis. She had a long history of headache and nasal obstruction and discharge. She improved by surgical debridement.

Surprisingly, both of our patients had perforated hard palate. The causative agents were *Cladosporium trichoides* (bantianum) and *Candida albicans*. Meanwhile, Wegner's syndrome and multiple myeloma were the possible predisposing factors in these two immunocompromised subjects.

DISCUSSION

During the recent decades, paranasal sinus mycosis has been recognized more frequently in different parts of the world thanks to the increased awareness of physicians. However, a significantly higher incidence was reported in the restricted zone of north Sudan, Saudi Arabia, the Middle East and in the south-western states of the USA, which have a warm and dry climate (5,6,10).

Central, western and southern part of Iran, including Sistan and Balochestan, Khozestan and Central provinces have similar climate during the summer months. Possibly the dust and frequent sand storms during the summer months contain large numbers of *Aspergillus* conidia that can easily settle on the injured mucosa of the sinuses in young men working outdoors who are exposed to the warm dry climate. In addition, the consumption of antibiotics (unwarranted at time), antihistamines and corticosteroids in the treatment of nasal allergy and sinusitis may play a role in the pathogenesis of the disease by suppressing bacterial flora and supporting fungal overgrowth. The maxillary and ethmoid sinuses were more commonly involved because drainage depends on mucociliary propagation in these sites (2).

It is interesting to study the reason why a particular fungus behaves in different ways in non-

immunocompromised patients resulting in the noninvasive and invasive types of fungal sinusitis. Jahrsdoerfer *et al.* have suggested that the distinction between the invasive and noninvasive forms of the disease is not clear (11). Jones and Gillon have proposed that paranasal sinus mycoses have a wide spectrum of manifestations, and that the invasive disease may develop from the noninvasive type and progress to the destruction of the bone (12). They felt that the duration of the disease might be important in determining the form of the disease which develops. Panda *et al.* suggested that invasive and noninvasive fungal sinusitis are two different disease processes (8).

The recently recognized noninvasive type of the disease with bone destruction (semi-invasive) represents a clinical spectrum in which bone destruction could be the end result of a long-standing disease in the sphenoid and frontal sinuses, causing hyperaemic decalcification with the resultant exposure of the dura (11).

Robb has reported a case of locally destructive aspergillosis that revealed tissue invasion only at the margins of the specimen (12).

In our series, *Aspergillus flavus* has been isolated more frequently than other agents, a finding that is in agreement with previous studies from north India and Sudan (5,13-16). *A. fumigatus* and *R. oryzae* have been found in an increasing number of cases (4,6,17). However, in allergic fungal sinusitis, *Biopolaris* (*Drechslera*), *Curvularia* and *Alternaria* were the predominant etiological agents in several studies (18,19).

Although the *Actinomyces* are now classified as bacteria, since their clinical and pathogenic characteristics resemble to those of fungi, they can be conveniently considered along with true mycotic infections. In our study, we isolated *Actinomyces* spp. in 22.2% of our patients.

The effective management of paranasal mycoses requires early diagnosis, histological classification, surgery and, when appropriate, chemotherapy (7). However, in patients with

zygomycosis, aggressive radical surgery is required along with medical therapy (20).

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