Paranasal Sinus Mycoses

Arunaloke Chakrabarti and Suresh C. Sharma[1]

Departments of Medical Microbiology and Otolaryngology[1], Postgraduate Institute of Medical Education and Research, Chandigarh

ABSTRACT

The incidence of paranasal sinus mycoses (fungal sinusitis) varies widely with higher frequency in Sudan, southwestern states of USA and north India, which have hot and dry climate. The disease has been described as having four types: allergic, non-invasive, invasive and fulminate. A possible fifth type: non-invasive destructive may also exist. In a prospective study of 176 cases of fungal sinusitis from our centre, on the basis of clinical, radiological, histopathologic and mycologic findings the patients could be categorized into: allergic (12), non-invasive without bone destruction (81), non-invasive destructive (16), chronic invasive (55) and fulminant (12) types. Except the fulminate variety, the disease is commonly found in young immuno-competent population of rural areas. *Aspergillus* spp. are the commonest etiological agents though the importance of dematiaceous fungi in allergic fungal sinusitis has been stressed. Zygomycetes are common agents in fulminate type. In our series A. flavus (80%) was the commonest isolate, followed by *A. fumigatus* (9.7%), *Rhizopus arrhizus* (6.3%) and *Alternaria* spp. (1.1%). *Curvularia lunata, Apophysomyces elegans* and *Candida albicans* were isolated from one patient each. Different host and environmental factors may help in lodging the causal fungi in mucosal plugs of these patients. Fungal allergy is associated with all varieties of the disease. But it is not clear what determines the invasion of mucosa. Rabbit can be used as an animal model. Histopathology and radio-imaging techniques help to distinguish different types and delineate extension of disease process. Culture helps to identify the responsible etiological agent. The presence or absence of precipitating antibody correlates well with disease progression or recovery. For effective management, non-invasive disease requires surgical debridement and sinus ventilation only. But for invasive type the need of adjuvant medical therapy is recommended to prevent recurrence and further extension. Itraconazole was found to be most useful in our study to prevent recurrence. Patients with fulminate type require radical surgery and immediate chemotherapy.

Key words : *Paranasal sinus, Aspergillosis, Animal model, Mycoses, Itraconazole.*

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INTRODUCTION

Fungal infection of the paranasal sinuses is uncommon. However, its incidence in recent years has shown a marked increase especially in northern Sudan, in southwestern states of USA and in north India[1-6]. It may present in one of the four forms: allergic, non-invasive (fungal ball), invasive (indolent) and fulminant types. Besides, an additional non-invasive destructive may be recognized[7,8].

Though species of *Aspergillus* are etiological agents in majority of such cases, dematiaceous

Correspondence : Dr Arunaloke Chakrabarti, Additional Professor, Department of Medical Microbiology PGIMER, Chandigarh - 160012.

hyphomycetes, *Pseudallescheria boydii*, *Candida* spp., *Fusarium* spp., hyalohyhomycetes and zygomycetes are also reported from some cases[2,6].

CATEGORIZATION OF PARANASAL SINUS MYCOSES

Oppe in 1897 described the first case of fungal sinusitis. In that case, the *Aspergillus* infection of sphenoid sinus had extended to cerebrum through erosion of the bony walls[9]. Wright in 1927 reported two more cases of invasive fungal sinusitis with extension to the orbit[10]. Categorisation of fungal sinusitis into two varieties was first suggested by Hora in 1965 : one non-invasive behaving clinically like chronic bacterial sinusitis and the other invasive, in which the infection results in a mass that behaves like malignant neoplasm, eroding bone and spreading into adjacent tissue[11]. However, no histologic evidence of invasion was provided in this report. Subsequently `invasive' cases have been reported when true fungal invasion has been demonstrated[12-14].

In 1980, McGill *et al* reported a third type of clinical manifestation of paranasal sinus mycoses in immuno-compromised patients: a fulminant form with a rapid, malignant course[15]. In 1981, Miller *et al* and in 1983 Katzenstein *et al* independently recognised pathophysiologic resemblance between few cases of chronic sinusitis associated with *Aspergillus* hyphae in mucosal plug of sinuses and patients with allergic bronchopulmonary aspergillosis, thus leading to a description of fourth type, namely allergic *Aspergillus* sinusitis[16,17]. Later it became apparent that dematiaceous fungi are also important etiological agents besides *Aspergillus* species[18,19]. Consequently, the name allergic *Aspergillus* sinusitis has been replaced by allergic fungal sinusitis (AFS)[20]. Recently, a chronic destructive form of paranasal sinus mycoses characterised by sinus expansion and bony erosion, but without any evidence of tissue invasion by fungi has been described[7,8]. Thus there are possible five different clinical types of fungal sinusitis, recognised today (Table 1).

A new classification has also been proposed to divide invasive fungal sinusitis into three varieties : fulminant invasive fungal sinusitis, chronic invasive fungal sinusitis and granulomatous invasive fungal sinusitis. The widely prevalent invasive fungal sinusitis of Sudan, Saudi Arabia and India with curious symptoms of chronic sinusitis, proptosis and noncaseating granulomas (granulomatous invasive fungal sinusitis) has been distinguished from other chronic invasive fungal sinusitis that has chronic course, dense accumulation of hyphae resembling mycetoma, and association with orbital apex syndrome, diabetes mellitus and corticosteriod treatment[21].

Table 1. *Categorisation of fungal sinusitis*

Category	Immune status	Role of fungus	Tissue invasion	Sinuses affected	Course
Allergic	atopic	allergen	No	multiple : unilateral	chronic
Mycetoma (fungal ball)	competent	saprophyte	No	one (usually)	chronic
Invasive (indolent)	competent (usually)	pathogen	Yes	variable	sub-acute
Fulminant	compromised	pathogen	Yes	one, ?multiple	acute
Destructive, non-invasive	competent	saprophyte	No	multiple	chronic, sub-acute

However, analysis of reports in the literature does not support such clear histologic distinctions of otherwise overlapping patterns of clinical manifestations of the disease. Jahrsdoerfer *et al*[12] have claimed that the distinction between invasive and non-invasive types is not clear-cut and Sarti and Lucente[22] proposed that the former type could develop from the latter. Both groups felt that the duration of infection was important in determining the form of disease that might develop. Therefore, fungal sinusitis may be considered as a potentially progressive spectrum of the disease[8]. However, during follow up of our large series of 176 cases, we did not observe any progression of non-invasive type to invasive type and the patients who came with recurrence presented with the same type as before[23].

ETIOLOGICAL AGENTS

The array of fungi which cause fungal sinusitis is broad (Table 2). Most of the fungi causing sinusitis are common saprobes. Different species of *Aspergillus* were found to be the causative agents of non-invasive and chronic invasive fungal sinusitis[2,6]. Most cases of *Aspergillus* sinusitis in Sudan and north India have been caused by *Aspergillus flavus*[2,4,62-64], but in the United States, *A. fumigatus* and *A. oryzae* have been found in increasing number of cases[5,6,11,65]. In one patient, *A. avanaceous* a fungus closely related to *A. flavus*, was implicated in the etiology of chronic invasive sinusitis[6]. Besides, the involvement of dematiaceous fungi particularly *Bipolaris* has been stressed by several workers[18,19].

In allergic fungal sinusitis *Bipolaris* (*Drechslera*), *Curvularia*, *Alternaria* are the predominant etiological agents[19,35,36,39,40]. Dematiaceous fungi were isolated from 88 out of 139 cases of allergic sinusitis reported till 1994[37]. But, in our series of allergic fungal sinusitis, we found *Aspergillus* species as the commonest agent[66].

The incidence of chronic invasive fungal sinusitis due to dematiaceous fungi has been increasing over the years and the diseases appear to manifest differently both clinically and pathologically[43,67,68]. Invasion was reported in 18 out of 39 cases of chronic invasive fungal sinusitis due to dematiaceous fungi[38,41,68,69]. Fulminant sinusitis due to zygomycetes and *Aspergillus* is well known because of the angio-invasive property of these fungi[2,15,30,47,48,70,71].

PATHOGENESIS

A variety of environmental and host factors have been held responsible for the development

Table 2. *Agents of paranasal sinus mycoses*

	Agents	References
I	**Narrow septate hyphae**	
	Hyaline mycelial fungi	
	Aspergillus spp.	1, 2, 4-8, 10-17, 22
	Pseudoallescheria boydii	3, 6, 24-26
	Fusarium spp.	27
	Paecilomyces spp.	28-30
	Penicillium spp.	31
	Schizophyllum commune	32
	Chrysosporium spp.	33
	Chaetomium spp.	34
	Dematiaceous fungi	
	Bipolaris spp.	18, 19, 35-38
	Curvularia spp.	37, 39-41
	Alternaria spp.	41, 42
	Exserohilum spp.	43
	Cladosporium spp.	44
	Stmphylium mucorsporidium	45
	Pleurophomopsis lignicola	46
II	**Broad non-septate hyphae**	
	Rhizopus spp.	2, 47-51
	Absidia corymbifera	52
	Apophysomyces elegans	53, 54
	Cunnighamella bertholletiae	55
	Conidiobolus coronatus	56
	Basidiobolus haptosporus	57
III	**Rounded structures**	
	Candida spp.	2, 58
	Cryptococcus neoformans	59
	Sporothrix schenckii	60
	Rhinosporidium seeberi	61

of fungal sinusitis. The common pathway in the conversion of these ubiquitous organisms from saprobic to pathogenic state is sinus obstruction with impaired ventilation in both normal individuals and immunosuppressed patients. Climate appears to be an important factor as higher incidence of fungal sinusitis has been reported from areas, which have a warm and dry climate[1-6]. Dusty, arid conditions predispose to rhinitis and recurrent sinusitis facilitates the growth of saprobic fungi. *Aspergillus* at higher concentrations was cultured from straw roofs, earthen floors, bedding and grains stored in the houses[64]. Summer sandstorms further disseminate the fungal spores leading to widespread saprobic colonization. Prolonged exposure of large inocula of spores, probably initiates even in immunologically normal host some degree of chronic sinonasal infection[2].

Several workers have stressed different host factors for predisposition of fungal sinusitis. Fulminant form is common in immuno-compromise [1] hosts. Other forms can occur in individuals without any underlying disease. Green *et al*[72] found only one out of 20 patients with orbital aspergillosis to have diabetes. Zinneman[73] did not find any systemic disease in a review of 37 sino-orbital cases. Alcoholic cirrhosis was identified in only one of 17 lethal cases[12]. Besides two cases of mucormycosis who had diabetes, none of the other 48 patients with fungal sinusitis from north India had any underlying disease[2]. Fulminant sinusitis occurs in patients with bone marrow transplantation, diabetes, malignant disease, burns and trauma but is not so common in patients on steroid or recipients of solid organ transplant[5,14,15,47,48]. AIDS, leukemia, Burkitt's lymphoma or head and neck primary malignancies as underlying disease have been stressed by some workers[74-76]. About 41% of 91 patients with acute lymphoblastic leukemia had abnormal sinus radiograph at the time of induction of chemotherapy[75]. Although leukemia or head and neck primary malignancy patients receive immuno-suppressive chemotherapy, the patients with leukemia tend to develop a profound mucositis facilitating the entrapment of fungal spores, which may cause fulminant infection[77-80].

Studies in rat suggest that a viral infection of the nasal airways enhances susceptibility to *Aspergillus* rhinosinusitis[81]. Fungal mycelium within a sinus can produce sinusitis either by acting as a foreign body or by producing a hypersensitivity reaction. However, it is strongly believed that hot, dry and dusty climate produce inflammation and mucositis, allowing an in-growth and tissue damage by the fungus and its metabolites, followed by the immunological reaction of the host to the fungal antigens leading to fungal sinusitis[2,14]. Both immediate and delayed hypersensitivity may be responsible in pathogenesis[2].

The possible role of excess dental root filling materials, which contain zinc oxide and paraformaldehyde from endodontically treated upper molar and premolar teeth, in inducing and stimulating antral aspergillosis was claimed by Beck-Mannagetta *et al*[82]. In a study of 34 otherwise healthy patients with *Aspergillus infection of maxillary sinus, a pathognomic* radiological appearance (within a homogeneously clouded antrum, one or more round to oval radiodense objects) was noted in 76% patients. All patients except one had a history of endodontic therapy[83]. The same group showed that soluble zinc promotes the growth of *Aspergillus* species, the effect diminishes with decreasing concentration[84]. In a patient, either zinc diffuses from area of endodontic therapy or it comes from exposure to dust or from antral foreign body that contains zinc.

The pathogenesis of allergic fungal sinusitis is not well understood. It has been suggested that the fungal elements trapped in the mucous in the sinus release antigenic material that stimulates IgE, IgG, IgA production[85,86]. What predisposes to the condition is not clear. Allergic fungal sinusitis may entail a pathophysiologic course similar to ABPA, with some initial insult causing accumulation of secretions and predisposing to fungal hypersensitivity. The inflammatory by-product of mast cell degranulation (Type I hypersensitivity) and immune complex tissue injury (Type III hypersensitivity) lead to further mucosal oedema and inflammation.

In an immuno-competent host, various factors may cause fungi to settle in mucous plugs of sinuses. The damaged mucosa fails to remove the foreign body and the fungal mass grows. Thus it stimulates granulomatous inflammation. But what determines the invasion of mucosa in some conditions is not clear. Whether fungal sinusitis is a potentially progressive disease in which a non-invasive stage gradually becoming semi-invasive and then invasive type, is yet to be established.

HISTOPATHOLOGY

Awareness of sinonasal mycotic disease is important for histologic diagnosis. The histopathology of different types of fungal sinusitis have been described by Brandwein[87] and Milory *et al*[31]. In acute fulminant form, the hyphae grow diffusely, however their fragmentation, swelling and degeneration make the hyphae less recognisable. Coagulative necrosis of the vessels may be seen, with hyphae growing in the lumen.

In chronic invasive form, there is a granulomatous response with considerable fibrosis. Noncaseating granulomata with foreign body or Langhans' type of giant cells may be seen, some with central microgranulomata of eosinophils. Some cases with narcotizing granulomata and extensive fibrinoid necrosis may also be seen. In many cases vasculitis, vascular proliferation and perivascular fibrosis are observed[14]. Hyphae on many occasions are scanty, appearing as holes in giant cells in routine stains, but can be identified with fungal stains.

In non-invasive form, a rhythmic centrifugal pattern of refractile hyphae or concentric layers like onion rings of thin hyphae may be seen with little inflammatory reaction. Conidiophores may also be seen. Hyphae do not have the same shape in all layers. Towards the centre of the fungal masses, they tend to appear swollen and bloated until they lose their structure altogether and seem to flow into each other.

In allergic fungal sinusitis, thick yellow or green inspissated mucous, which is difficult to remove from sinus cavity is seen with typical nasal polyp. The `allergic' basophilic or eosinophilic mucin contains sloughed respiratory epithelium, chronic inflammatory cells with prominent eosinophils, and Charcot-Leyden crystals. Fungal hyphae remain scanty and are not easily visualized in routine stain but can be identified by fungal stains.

ANIMAL MODEL

Paranasal sinus mycoses can be experimentally induced in rabbit by direct inoculation of 0.75-1.0 $\times$ 10^8 conidia of *A. flavus* at a spot 0.5 cm in-front of alveolar process of maxilla and 0.5 cm below the maxillary process of frontal bone and vertically to a depth of 0.5 cm across the bone directly into the nasal sinus[88]. But similar trials to develop fungal sinusitis in mouse or rat have not succeeded in simulating the disease except in a study rhinitis was developed in Wistar rat[81].

CLINICAL FEATURES

Fungal sinusitis has been described as a disease process that primarily affects young male farmers[2] though the mean age of the patients from Mayo Clinic was significantly higher than those previously reported[37]. The most common non-invasive form of fungal sinusitis presents as chronic sinusitis, unresponsive to conservative medical treatment and repeated sinus irrigations. Encountered in immuno-competent individuals, this form of disease presents with rhinorrhae, nasal obstruction, and headaches.

Allergic fungal sinusitis accounts for approximately 6% to 8% of all chronic sinusitis. Patients not only have functional immune systems but also have positive history of atopy. Nasal polyps are seen in almost all cases and the disease generally affects multiple sinuses although unilateral manifestation predominates. Most patients report with a history of long-standing chronic sinusitis. Acute worsening of chronic condition with nasal obstruction and headache typically draws the attention of

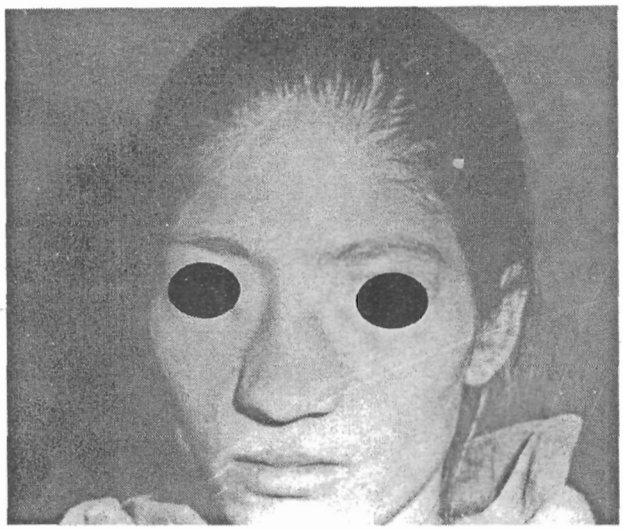

Figure 1. Marked telecanthus and proptosis due to extension of lesion from bilateral pansinusitis (invasive *Aspergillus* sinusitis).

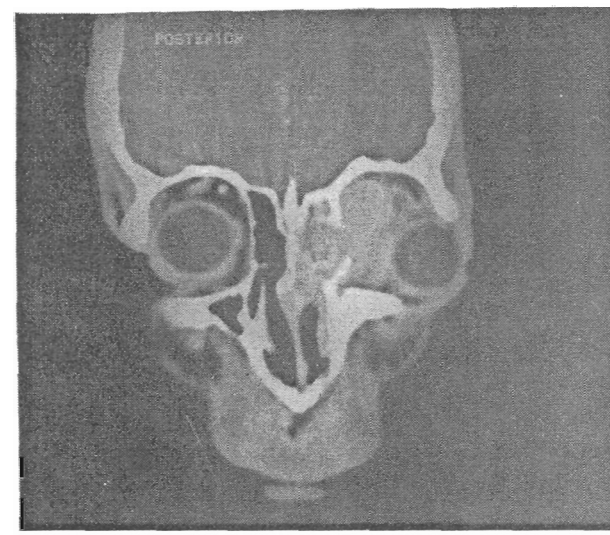

Figure 2. Coronal CT of paranasal sinus and orbit showing an infiltrating mass involving ethmoids and orbit with loss of tissue planes (invasive fungal sinusitis).

otolaryngologists. Orbital symptoms or proptosis occur in some patients with impaired vision[66,90]. According to reports published from Mayo Clinic[37] nasal obstruction, local pain and rhinorrhea are the common presenting symptoms.

Patients of chronic invasive fungal sinusitis present clinically with an enlarging mass in cheek, orbit, nose and paranasal sinus regions (Fig. 1). Proptosis is often a prominent feature[2]. The disease usually follows a relentless course over months or years of insidious erosion of anatomic barriers. With intra-cranial extension there may be frontal lobe symptoms or signs including chronic headaches, localizing neurological findings, seizures, altered sensorium and urinary incontinence. Chronic destructive variety may present exactly like chronic invasive type either with proptosis or with bitemporal headache, facial pain, cachosmia[7].

Acute fulminate type is found in immunocompromised individuals and has the highest morbidity and mortality. In the initial stage, there may be mild symptoms like fever and headache but within no time it presents with black crusting of turbinate, nasal septum and spreads rapidly to surrounding structures leading to swelling of soft tissues, proptosis, blindness, conjugal chemosis, ophthalmoplegia, signs and symptoms of meningeal involvement or intracranial space occupying lesion and cerebral infarction. Spread along base of skull is associated with multiple cranial nerve palsies. Extension into cranial fossa is usually fatal. In a 10 year review of leukaemic patients, Talbot *et al*[80] found that a persistent pyrexia was the most common presenting feature (100%), with cough (64%), crusting of the mucosa (75%), epistaxis and headache (50% each), followed by nasal discharge, sinus pain, tenderness and a sore throat.

RADIOLOGY

The radiological diagnosis of fungal sinusitis on plain x-ray is difficult. A nodular mucosal thickening and the absence of air/fluid levels in homogeneously cloudy maxillary and ethmoidal sinuses, with or without bony destruction, have been described. Occasionally expansion of maxillary sinus or lateral displacement of lamina paparacia suggest PNS mycoses. Unusual air/fluid levels seen in plain x-ray of immunocompromised patients with *Aspergillus* sinusitis have also been described[80]. The presence of hyperdense fungal concretions on plain x-ray is almost pathognomic of fungal sinusitis. These concretions may be calcium deposits or

represent zinc oxide following endodontic treatment[5,82,83].

Both CT and MR images help in the clinical diagnosis of fungal sinusitis, its recurrence and delineating its extension (Fig. 2) as well as in surgery[91]. Radiologically there is total opacification of one or several sinuses. In a comparative CT and MR imaging study, Zinreich *et al*[92] reported that the more highly inspissated mucus present in cases of fungal sinusitis showed greater attenuation (a mean of 122 Hounsfield units) than in cases of bacterial sinusitis. With MR imaging, decreased signal intensity was noted, especially in T2-weighted image. This was attributed to increased levels of magnesium, manganese and iron in mucinous contents of the sinuses.

Patients with non-invasive fungal masses generally exhibit increased soft-tissue density in only one sinus. Stammberger *et al*[5] claimed that calcium phosphate deposition with *Aspergillus* masses can produce dense opacities on CT scan. Extension of soft tissue in contiguous structures such as orbit or brain is indicative of invasion. However, in sinuses itself, it is difficult to distinguish between non-invasive and invasive fungal sinusitis except that in non-invasive type the intersinus septa in ethmoid labyrinth are intact (Fig. 3), whereas in invasive type, these are destroyed. The resolution obtained by MRI is better than CT. But inability to see bony details has prevented MRI from replacing CT for diagnostic imaging in fungal sinusitis. The best way to identify bony destruction is by CT. However, MRI is also desirable to provide information about areas of critical importance, such as cavernous sinuses and brain[5,80,92].

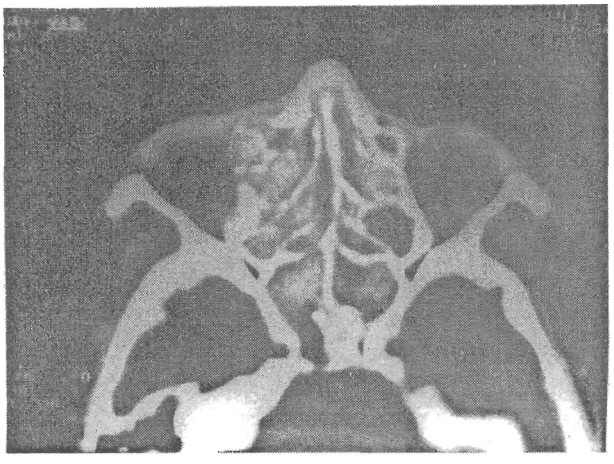

Figure 3. Axial CT of paranasal sinus showing mass of variegated consistency involving bilateral ethmoids and sphenoid sinuses with intact inter sinus septa. The mass has destroyed lamina paparecea without infiltrating the surrounding tissue (non-invasive, destructive type of fungal sinusitis).

DIAGNOSIS

Fungal sinusitis should be considered in all patients with chronic sinusitis, especially in association with certain clinical features like intractable symptoms despite adequate treatment for bacterial sinusitis, allergic rhinitis, asthma, nasal polyposis, (non-invasive types) or fever, headache, epistaxis, diabetes, nasal mucosal ulcer, orbital apex syndrome, proptosis (invasive types)[21]. However, the diagnosis of the fungal sinusitis depends on direct microscopical examination, culture and histopathology of tissue or the cheesy material obtained from sinuses. Direct microscopy helps in diagnosis of fungal etiology and culture helps in identification of the etiologic agent. Histopathology is important to distinguish the invasive from the non-invasive type. The distinction is easier and can be diagnosed even clinically when invasion of contagious structures has occurred. But when the lesion is restricted to the sinus, demonstration of histopathological invasion of mucous membrane is the only criterion to rely on. For the diagnosis of allergic fungal sinusitis, the following criteria should be met : Type I hypersensitivity, nasal polyposis, characteristic computed tomography showing serpiginous areas of high attenuation in affected sinuses, eosinophilic mucous without fungal invasion and positive fungal culture of sinus contents removed during surgery[20].

Several immunological tests are performed to evaluate host defenses with fungal sinusitis. Precipitin antibody detection and skin test especially against *Aspergillus* helps in preliminary screening of patients[2].

Table 3. *Fungal isolated from different types of paranasal sinus mycoses in north India*

Agents	Allergic	Non-invasive*	Chronic invasive	Fulminant	Total (%)
Aspergillus flavus	9	81	50		140 (79.5)
Aspergillus fumigatus	1	12	4		17 (9.7)
Aspergillus niger	1	-	-		1 (0.6)
Aspergillus spp.	1	1	-		2 (1.1)
Alternaria spp.	-	2	-		2 (1.1)
Curvularia lunata	-	1	-		1 (0.6)
Rhizopus arrhizus	-	-	-	11	11 (6.3)
Apophysomyces elegans	-	-	-	1	1 (0.6)
Candida albicans	-	-	1		1 (0.6)

*16 patients in this group of non-invasive fungal sinusitis had bony destruction without mucosal invasion and those patients may be considered under non-invasive destructive type.

MANAGEMENT

The effective management of paranasal sinus mycoses requires proper diagnosis, its histological classification, surgery and where appropriate chemotherapy. Surgery is the initial treatment and the objectives are debridement, wide aeration of infected sinus and providing specimen for histological and microbiological study. After confirmation of diagnosis, the planning of definitive surgery is required. In non-invasive type, surgery may be all that is required. In invasive disease, chemotherapy is also required. In fulminant type, the role of surgery is less certain as the patients are usually neutropenic and thrombocytopenic[80,93].

The issue of adjuvant medical therapy in invasive disease is still unresolved. However, majority of workers feel that medical therapy in conjunction with surgery in invasive disease prevents recurrence and further extension of disease[6,14,64,93]. Systemic amphotericin B is the antifungal drug of choice. Now preparation of amphotericin B - liposomal or lipid complexes can be given at much higher concentration than free amphotericin B as the former is less toxic. Combination of amphotericin B and 5-fluorocytosine has been recommended by Arroyo *et al*[94] and 5-fluorocytosine is effective against some of the dematiaceous fungi. Topical amphotericin B by intraoperative sinus irrigation or repeated packing of the antral cavity with amphotericin B soaked ribbon gauze has also been reported[68,95]. Because of known toxicity of amphotericin B, alternate therapy by azoles has gained importance, especially with itraconazole[68,93]. Ketoconazole has been used earlier in patients with *Pseudallescheria boydii* infection[3]. Rowe-Jones and Moore-Gillon recommended oral itraconazole in addition to surgery in-patients with destructive non-invasive fungal sinusitis[7]. Saperconazole may also be a valuable alternative[96]. Systemic corticosteriods have been proposed in the management of allergic fungal sinusitis, extrapolating from the experience gained from allergic bronchopulmonary aspergillosis. However, surgery alone may be curative in allergic fungal sinusitis[19,68].

WORK DONE IN INDIA

North India has been identified as an endemic zone of paranasal sinus mycoses[2,23,63,66,97,98]. In last ten years more than 200 cases are reported from our centre[2,23,63,66]. Concomitant allergic bronchopulmonary aspergillosis with allergic *Aspergillus* sinusitis, a rare association, was reported from Delhi in two patients[99,100]. Fungal sinusitis is most common in young farmers of north India[2, 23]. In a prospective study of 176 cases of fungal sinusitis from our centre, *Aspergillus flavus* was found to be the causative agent in 80% of the patients. The remaining fungi cultured were *A. fumigatus* (10%), *Aspergillus* spp., *Alternaria* spp., *Curvularia lunata*, *Rhiz-*

opus arrhizus, *Apophysomyces elegans* and *Candida albicans* (Table 3). On the basis of clinical, radiological, histopathologic and mycologic findings the patients could be classified into following types: allergic (12 patients), non-invasive without bony destruction (81), non-invasive destructive (16), chronic invasive (55) and fulminant (12)[23].

Regarding pathogenesis, both immediate hypersensitivity and delayed hypersensitivity may be important as immediate hypersensitivity was detected in 96.6% of patients with non-invasive variety and 92.9% with invasive variety and Type IV hypersensitivity in 31% with non-invasive variety of sinusitis when *Aspergillus* species were isolated[2]. In the evaluation of immunological tests, precipitating antibody is found to predict the course of the disease. In a study from north India, precipitin became negative or diminished in intensity or in titer after 2-3 weeks of surgery in 11 (92%) out of 12 patients; it reappeared in-patients with recurrence or progression of lesions[2]. Skin test and IgE estimation help in understanding the atopic state of the patients as most of the patients with fungal sinusitis show immediate hypersensitivity or raised IgE against antigen of the etiological agents[2]. Recently, animal model of paranasal sinus mycoses is developed in rabbit for the study of pathogenesis of this disease[88].

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