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Fungal sinusitis An Overview

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Abstract:

Fungal infections of nose and paranasal sinuses are getting common these days. Nose and paranasal sinuses being constantly exposed to environmental insults causing them to be infected. With increasing incidence of diseases like HIV and life style disorders like Diabetes Mellitus compromises host immunity, that it is no wonder that the incidence of fungal infections involving the nose and sinuses are on the rise. In addition the incidence of fungal infections in immunocompetent persons are also on the rise. This article attempts to review the published literature available on this topic concurrently along with our experience on this subject. In Indian scenario the incidence of fungal infections involving the nasal cavity has shown an increase. There is also a significant increase in the incidence of fungal infections involving the nose and sinuses even in immunocompetent individuals. Increased use of advanced imaging techniques like CT scan, MRI, and Nasal endoscopes have increased the awareness of Rhinologist to this disease spectrum.

Definition:

Fungi are eukaryotic organisms comprising of moulds, yeasts, mushrooms and other similar organisms. Among this group of organisms only about 0.1% are human pathogens [1]. The term mycosis is used to define diseases caused by fungi.

Mycosis can be classified under 4 heads based on the portal of entry and site of infection [2].

The number of fungal species have been estimated somewhere between 20,000 – 100,0000. This variation indicates clearly our lack of knowledge about the various fungal species involved in human infections. Studies indicate about a dozen fungal species to be actively involved in human infections. Classically fungi exists in two forms:

1. Yeast form

2. Mold form

3. Spore form

Yeast form of fungi are usually unicellular measuring roughly about 3-15 μm in diameter. Yeast forms multiply asexually by a process known as budding. These buds detach to form new fungi. In some species these buds dont detach, instead they form chain of fungi. This chain is known as pseudohyphae.

The Mold is a multicellular organism measuring 2-10 μm in diameter. These fungi grow by branching into structures which are termed as hyphae.

Spore form is a reproductive form of fungus, which occurs during unfavorable conditions. Major feature of these spores is their ability to withstand harsh environment. They simply tide over the period of harsh environment waiting for favorable environment. When environment becomes favorable these spores begin to germinate. Studies reveal that inhalation of these spores is the major cause for rhino sinus mycosis.

Types of Mycosis:

Type	Pathophysiology	Route	Example
Superficial	Limited to keratinized tissues	Topical	T. pedis
Subcutaneous	Localised to subcutaneous tissues	Broken skin	Rhinosporidiosis
Systemic	Disseminated widely	Inhalation	Histoplasmosis
Opportunistic	Local / Disseminated	Cell mediated immunity compromise	Candida / Mucormycosis

Exposure to fungal organism occur on a daily basis. Our immune system invariably tackles the initial fungal infections. In some patients fungal infections may become invasive leading to disastrous consequences. Hence it is very important for the treating physician to differentiate invasive fungal infections from non invasive ones.

Classification of fungal sinusitis [3]:

Broadly fungal infections involving paranasal sinuses can be classified under two broad categories.

1. Non invasive – Saprophytic infections, fungal ball, allergic fungal sinusitis

2. Invasive – Acute fulminant invasive sinusitis, Chronic invasive sinusitis and granulomatous invasive fungal sinusitis.

Clinically 6 different types of fungal sinusitis have been described depending on the pathophysiology and clinical features:

1. Acute fulminant invasive fungal sinusitis

2. Chronic invasive fungal sinusitis

3. Granulomatous invasive fungal sinusitis

4. Fungal ball

5. Allergic fungal rhinosinusitis

6. Eosinophilic fungal rhinosinusitis

Acute fulminant invasive fungal sinusitis:

The entire duration of illness in these patients is less than a month. These patients are invariably immunocompromised. Immune compromise could be due to:

a. Diabetes mellitus

b. AIDS

c. Patients on immunosuppresive medicines

d. Patients with malignancy causing immunosuppression

Acute fulminant invasive fungal sinusitis is caused by fungal infections due to:

1. Mucoracea family – seen under microscope as broad hyphae which very rarely septates. Branching out is seen at right angles. This is clearly seen under methanamine / PAS staining of the tissue.

2. Aspergillous family – seen under the microscope as narrow and septate hyphae. Branching could be seen to occur at acute angles.

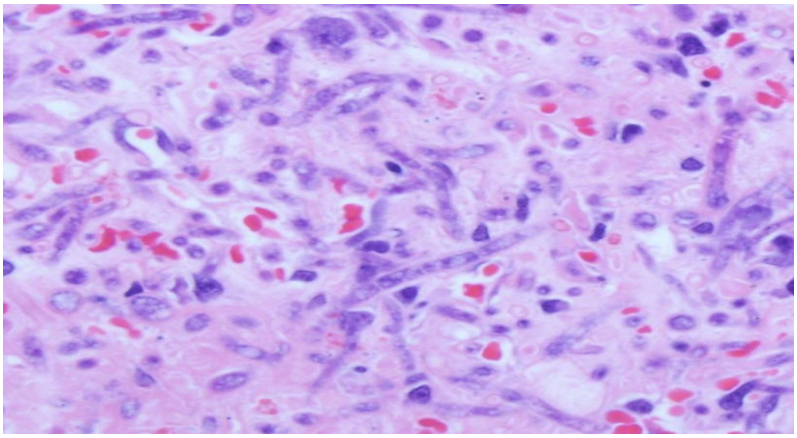


Figure showing mucormycosis under High power

If mucor is the offending pathogen then it is angioinvasive causing extensive destruction of bone and soft tissue. These patients have a very high mortality rate [5].

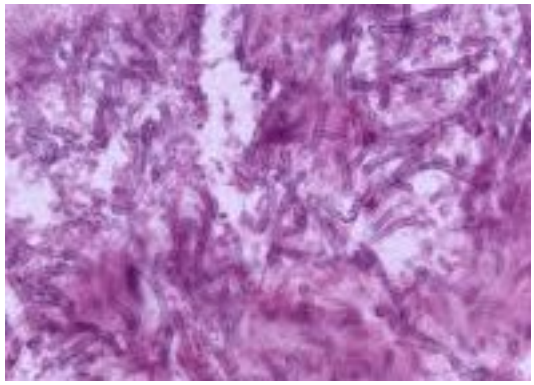


Figure showing aspergillosis

Considering the amount of tissue necrosis involved in these patients, surgical debridement followed by intravenous antifungal medications (amphotericin B) is the treatment of choice. This should also be associated with good euglycaemic control. Since granulocytes are necessary in combating this condition, granulocyte transfusion [4] has been attempted with certain degree of success in these patients following wound debridement.

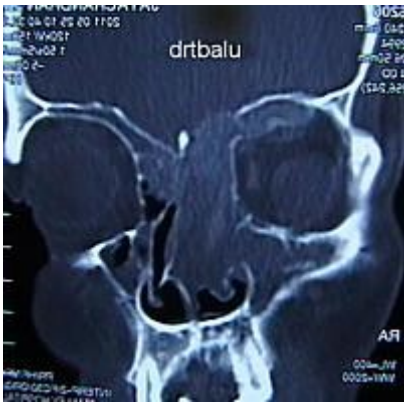
Chronic invasive fungal sinusitis [6]:

This condition is also known as non granulomatous chronic invasive fungal sinusitis. This condition is commonly seen in patients with diabetes mellitus. Feature of this infection is low grade inflammation with tissue necrosis. Usually this disease lasts between 4-6 weeks. Vascular invasion is not seen. Granuloma formation is classically seen. Orbital involvement (Orbital apex syndrome)is common in these patients. This condition affects immunocompetent patients. Fronto ethmoidal region is commonly involved. Maxillary sinus and sphenoid sinus are very rarely affected. More than 80% of these patients have fronto ethmoidal sinus involvement. Aspergillosis have been implicated as the commonest pathogen involved [8].

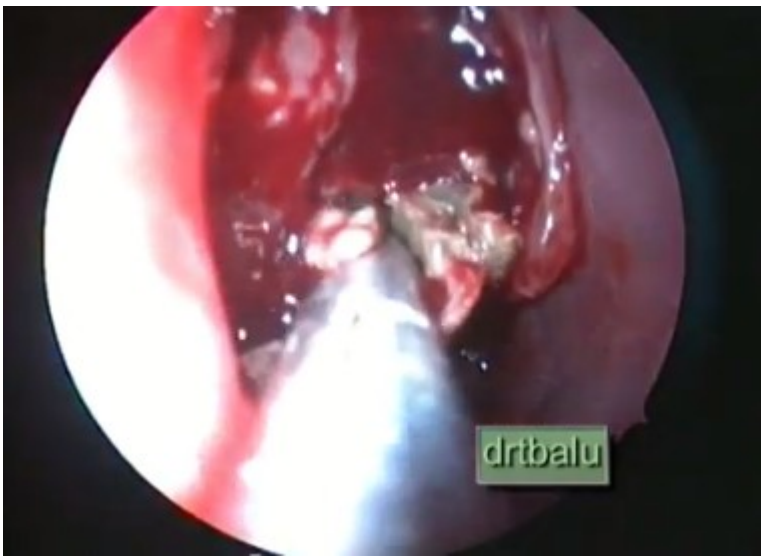
Orbital apex syndrome is characterised by:
1. Decrease in vision
2. Ocular immobility
3. Proptosis

Ideally these patients are managed by surgical debridement followed by systemic antifungal drugs like amphotericin B infusion.

Chronic invasive fungal sinusitis is rather rare. According to Ferguson (2005) it constitutes less than 0.003% of all forms of fungal sinusitis operated on.



CT scan coronal cut nose and sinuses of a patient with chronic invasive fungal sinusitis with orbital involvement



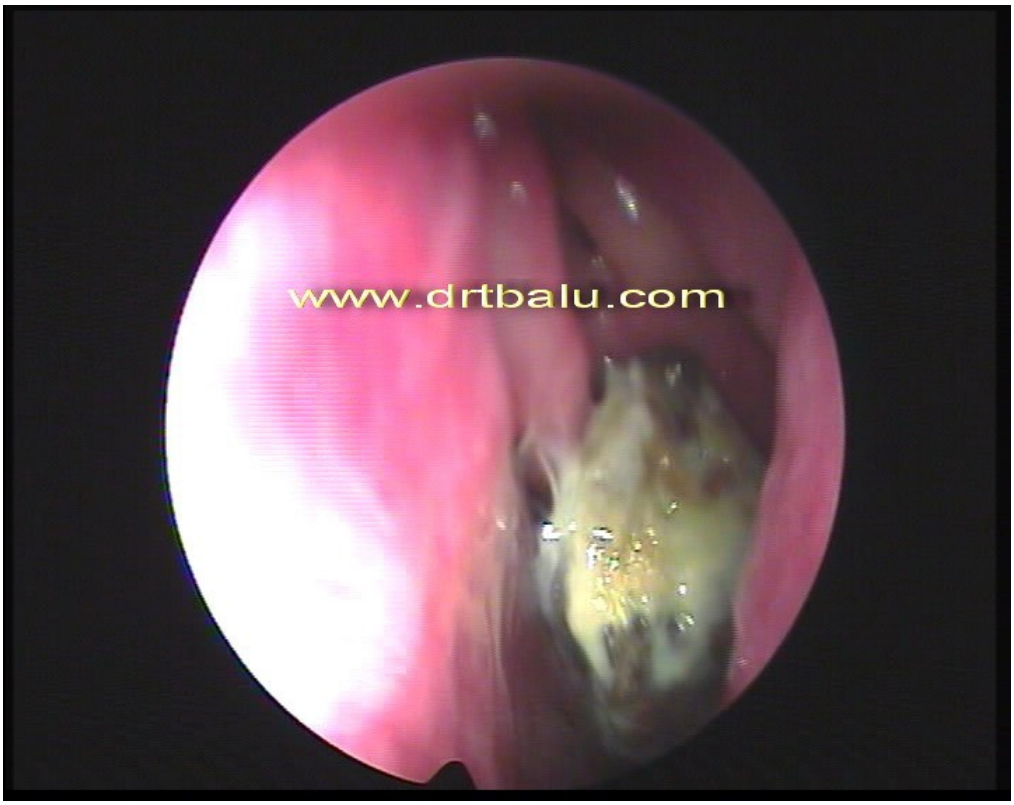
Endoscopic view of chronic invasive fungal sinusitis

Granulomatous invasive fungal sinusitis:

This condition is also known as “Indolent fungal sinusitis”. Classically these patients have intact cell mediated immune response. These lesions are caused by Aspergillus flavous Clinically this condition is indistinguishable from chronic invasive fungal sinusitis. This is actually a histopathological entity. The intact cell mediated immunity limits the lesion to he surface mucosa. Granulomas could be seen surrounding the fungal elements there by effectively preventing their invasion. Granulomas typically non caseating and demonstrate the presence of multinucleated giant cells and eosinophils. This condition is effectively managed by surgical debridement. After successful wound debridement the intact immune system takes care of the disease. Treatment with itraconazole / varioconazole has shown promising results.

Fungal Ball:

These are also known as mycetomas. Mycetomas commonly present as unilateral opacification of maxillary / sphenoid sinuses. This condition is rather rare in ethmoid and frontal sinuses [9]. Fungal ball is composed of tightly packed hyphae mostly from (aspergillus, alternaria and P. Boydii).



Endoscopic image showing fungal ball coming out of the middle meatus

This is actually a sequestration of fungal hyphal elements within the sinus without any invasive / granulomatous changes. Nasal mucosa is absolutely normal in these patients.

This disease is classically caused due to inhalation of spores, which eventually gets sequestered either into maxillary or sphenoid sinuses. Fungal growth occurs within the confines of the affected sinus cavity. Fungal growth occurs because of the ability of the infecting pathogen to avoid host immune response.

Signs and symptoms may mimic chronic rhinosinusitis in advanced cases. Clinical examination reveals very little. CT imaging reveals opacity of the involved sinus cavity.

This condition is managed by surgical removal of the fungal ball and creating good ventilation to the involved sinuses by widening the sinus ostium. Systemic antifungal agents are not indicated in these patients. Topical antifugal agents have been administered with varying degrees of success.

In majority of these patients this condition was diagnosed as an incidental finding when routine imaging of nose and sinuses were performed.

Allergic Fungal sinusitis:

This rather poorly understood entity was first reported in 1976 [10]. In 1983 Katzenstein et al described a condition and coined the terminology allergic aspergillus sinusitis. They made the diagnosis based on the presence of histological triad of "clumps / sheets of necrotis eosinophils, Charcot – Leyden crystals probably from degenerating eosinophils and non invasive fungal hyphae resembling aspergillus species. These patients have a combination of nasal polyposis, crust formation and positive culture for aspergillus. It was Robson in 1989 [11] who introduced the term allergic fungal sinusitis to describe the findings associated with this disease. According to Cody aspergillus species was responsible for only 15% of allergic fungal sinusitis. This was evident from the retrospective study conducted by him covering a large sample size [12].

Incidence of allergic fungal sinusitis among chronic sinusitis is placed around 6-7% [13].

Based on clinical findings Bent and Kuhn proposed certain criteria for diagnosis of allergic fungal sinusitis.

Bent's criteria [14] for the diagnosis of allergic fungal sinusitis:

1. Demonstrable type I hypersensitivity to fungi
2. Nasal polyposis
3. Radiological findings (Heterodense mass lesion)
4. Presence of eosinophilic mucin mixed with non invasive fungus
5. Positive fungal stain / fungal culture

Swain's modification [15] of Bent's criteria:

deShazo and Swain slightly modified the diagnostic criteria laid out by Bent. They left out the type I hypersenitivity criteria alone since only 2/3 of patients with allergic fungal sinusitis manifested with hypersensitivity to fungal protein in various studies.

Bent and Khun modified their diagnostic criteria for diagnosis of allergic fungal sinusitis by adding major and minor diagnostic criteria.

Major criteria	Minor criteria
Type I hypersensitivity	Asthma
Nasal polyposis	Unilateral disease
Charactersitic CT findings	Bone erosion
Eosinophilic mucin	Fungal cultures
Positive fungal stain	Charcot Leyden crystals and eosinophilia

Undisputed diagnostic criteria for the diagnosis of allertic fungal sinusitis include:

1. Chronic rhinosinusitis

2. Presence of allergic mucin

3. Presence of fungal organism within the mucin

Allergic fungal sinusitis like condition:

In this category those patients who do not demonstrate positive fungal presence in the mucin or in cultures of mucin are included. The paucity / absence of fungal elements in these patients could be accounted for by the presence of increased amounts of major basic protein released by eosinophils. Major basic protein has been found to be toxic to fungi [17].

Clinical features of allergic funcal sinusitis:

These patients present with progressive nasal obstruction, crusting, rhinorrhoea, and chronic rhinosinusitis. These patients can also come with dramatic symptoms like visual loss and total nasal obstruction.

Classically radiology shows unilateraly expansile lesion of the sinuses associated with bony erosion. The mass appears as heterodense due to the presence of metallic elements in the fungal hyphae. Unilateral asymmetric involvement of sinuses is the classic feature of this condition [16].

The mechanism of causation of allergic fungal sinusitis is IgE mediated hypersensitivity to fungal proteins especially to aspergillus. Both type I and type III hypersensitivity reactions to fungal proteins have been implicated. Allergic fungal sinusitis still remains an under reported condition due to lack of awareness amongst treating physicians.

Expansile lesion involving the right maxillary sinus. Erosion of medial wall of maxilla, the nasal cavity is filled with heterodense mass. The septum is seen being pushed to the opposite side.

Endoscopic staging of allergic fungal sinusitis:

Endoscopic Picture	Staging
No mucosal oedema / allergic mucin	0
Mucosal oedema with / without allergic mucin	1
Polypo formation with / without allergic mucin	2
Polyposis with fungal debris and allergic mucin	3

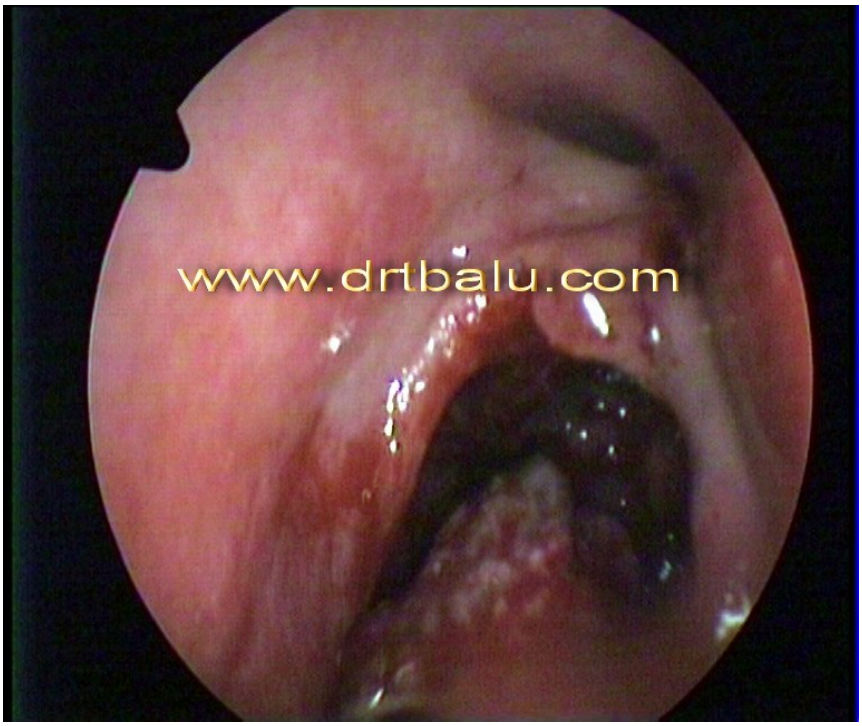
This condition is best managed by surgical removal of mucinous element and providing lasting drainage and ventilation to the involved sinuses. Administration of systemic steroids helps in reducing the incidence of recurrence in these patients as this condition is attributed to immunological reaction to fungal protein.
Currently immunotherapy has shown promising results in these patients.

Eosinophilic fungal sinusitis:

This terminology was introduced by Ponikau etal to explain pathophysiology of chronic sinusitis. This disorder is usually bilateral. Fungal hyphae has been demonstrated in almost all these patients. Studies have not manged to demonstrate increased levels of IgE in these patients. Hypersensitivity reaction has been ruled out as a cause for this type of fungal sinusitis. It has been postulated that this condition could be caused by abnormal cell mediated immunity to fungal proteins.

These patients respond well to surgical removal of polypoidal mucosa, and creation of wide

antrostomy which improves ventilation to the sinus mucosa.



Endoscopic view of fungal sinusitis

Conclusion:

With increasing awareness of fungal infections and reactions to it in the nasal cavity and paranasal sinuses a large number of these cases are being reported. Advent of nasal endoscopy and advanced imaging techniques are playing a vital role in managing these patients.

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