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DIAGNOSTIC ROLE OF HISTOPATHOLOGY IN FUNGAL SINUSITIS

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ABSTRACT

Background: Acute or chronic rhinosinusitis is a common condition affecting upto 20%of the population. Fungal organisms are one of the proposed aetiological agents and are seen in 6-12 % of these patients.
Objective: To categorising the fungal sinusitis according to the classification & studying the histomorphology of fungus
Methods and Material: A retrospective analysis of 65 cases of fungal sinusitis were studied for 1yr at Department of Pathology, Madras Medical College. On histopathological evaluation the cases were classified as Non invasive and invasive fungal rhinosinusitis (FRS) depending on tissue invasion.
Results: Three histologic categories of FRS were identified:1) Mycetoma/fungal ball (70%). 2)chronic invasive FRS (18.4%). 3) chronic granulomatous invasive FRS (2%). Oppurtunistic infections like DM was present in 29% and remaining cases were immunocompetant. Aspergillus was most common fungal species seen in fungal ball and mucormycosis was common in chronic invasive FRS and chronic granulomatous invasive FRS. Angioinvasion waspresent in 6 cases of mucormycosis

Introduction

Fungal Rhinosinusitis (FRS) has been a known medical entity for several hundred years but only in more recent times, the entity has been further defined. Disease is most commonly classified as benign non-invasive or invasive based on whether the fungi have invaded into the submucosal tissue resulting in necrosis and tissue destruction.[1-3] Non invasive can be further divided into two forms: allergic fungal sinusitis (AFS) and Sinus mycetoma/ fungal ball with occurs in immunocompetent patients. AFS should be suspected in individuals with intractable sinusitis and recurrent nasal polyposis. These patients usually have atopy. Computerised Tomography (CT) scans of the sinuses reveal opacification with concretions and/or calcification.[4] Invasive disease is characterised by acute or chronic based on duration of symptoms. Patients with acute invasive disease (AIFRS) are usually immunosuppressed and, by definition, present with symptoms of less than one-month duration. This entity is characterized by the presence of fungal forms invading into the sinonasal submucosal tissue with frequent angioinvasion and rapid intervention is necessary. Patients with chronic invasive disease present with symptoms of greater than three months duration. Two forms of chronic invasive disease, chronic invasive FRS (CIFRS) and chronic granulomatous FRS (CGFRS), have been described and like AIFRS both are serious, often requiring surgical and medical therapy.[5] Accurate classification of FRS is important because prognosis and treatment varies among FS diagnosis. Although the clinical presentation may provide diagnostic clue for each category, only tissue examination can provide accurate classification.[6]This study aims at categorising the fungal sinusitis according to the classification, studying the histomorphology of fungus and associated tissue reaction to the fungus.

Table 1: Classification of fungal rhinosinusitis based on Histopathologic criteria[5]

NON INVASIVE	INVASIVE
Fungal ball : An entangled mass on fungi with Minimal surrounding inflammatory reaction or surrounding fibrinous necrotic exudates containing fungal forms; No tissue invasion or granulomatous reaction is present	Acute (AIFRS) Invasion of fungal forms into submucosal with frequent angioinvasion and necrosis in a patient with symptoms of less than one month duration.
Allergic fungal rhinosinusitis (AFRS) The presence of eosinophilic mucin (mucinous material admixed with eosinophils, acute inflammatory cells, eosinophilic debris, and charcot leyden crystals; sparse fungi or positive fungal cultures; no tissue invasion present)	Chronic (CIFRS) Invasion of fungal forms into submucosa often with surrounding chronic Inflammation and fibrosis in a patient with long standing symptoms (>3months duration)
Mixed FB/AFRS The presence of features of both AFRS and FB	Chronic granulomatous (CGFRS Invasion of fungal forms into submucosal often with surrounding chronic inflammation, fibrosis, and granuloma production in patients with long standing symptoms (>3months duration)
Mixed non invasive / invasive FRS A mixture of either of the invasive and non invasive categories	

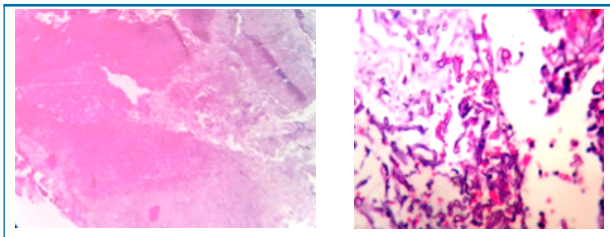
Materials And Methods

A retrospective analysis of 65 cases of fungal sinusitis was included in the study from Jan 2017 to dec 2017 at department of pathology, Madras Medical College, Chennai. Relevant clinical details and, radiological details if any, were analysed. Conventional haematoxylin and eosin stained sections along with special stains, per iodic acid Schiff & Grocotts methenamine silver (GMS) stain were examined. The cases were classified as Non invasive and invasive fungal sinusitis depending on tissue invasion. The morphology of the fungus and H&E visibility of fungus were studied. Tissue reactions like degree of inflammatory infiltrate, granulomatous response and tissue necrosis associated with fungus were assessed.

Observations

Of the 65 cases of FRS, ages of the patients ranged from 19 to 72 yrs. There was predominance of FRS in male patients with male: female ratio of 1.4:1. Oppurtunistic infections like Diabetes mellitus was present in cases (29%). Remaining cases were immunocompetent.

On Histopathological examination, cases were broadly categorised as (I) Non invasive FRS (n=46)cases-(70%) all of which were diagnosed as fungal ball (70%), None of the cases were allergic fungal sinusitis in our study. (II) Invasive FRS (n=19 cases, 29%) includes chronic invasive fungal sinusitis in 12 cases (18.4%), chronic granulomatous invasive FRS in 1 cases (2%) and Acute fulminant (acute invasive FRS) in 6 cases (9%) Fungal Ball (Mycetoma) (46 cases, 70%) This was characterised by tightly packed fungal hyphae appearing pale in the centre with morphology more apparent on the periphery. The adjoining mucosa showed a mild mixed inflammatory infiltrate. Of which 33 cases of mycetoma were associated with Aspergillus, having thin septate acute-angle branching hyphae (fig, 1A), 10 cases were mucormycosis have broad,aseptate obtuse angle branching hyphae (fig 1 B)and 3 cases were mixed(aspergillous & mucormycosis).

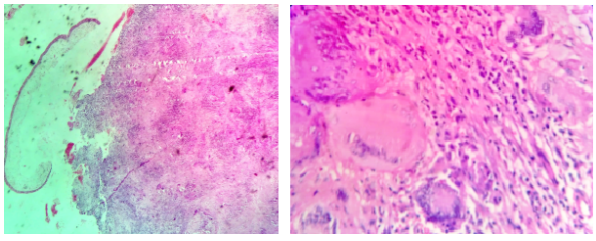


A B

Figure 1. A)Tightly packed hyphae of Fungal ball (non invasive). Fungi appears as homogenous eosinophilic masses. (H & E stain) B) PAS stain: shows broad aseptate fungal hyphae

Chronic Invasive FRS (12cases, 18.4%)
This showed tissue invasion of fungal hyphae and severe acute inflammatory infiltrate, foci of necrosis and scattered giant cells. All were found to be mucormycosis. one case of Chronic Granulomatous invasive FRS (2%) caused by mucormycosis was reported.

This condition showed multiple granulomatous inflammation (fig:2) involving the mucosa with fungal hyphae seen within the splendore-hoeppli reaction.



10x 40x

Figure: 2 10x and 40x shows multiple granulomatous inflammation

Acute Fulminant FRS (n=6cases-9%)

Out of which 4 cases presented with headache, periorbital swelling and Defect in vision and 2 were presented with facial nerve palsy. There was extensive areas of coagulative necrosis, mild inflammatory infiltrate and evidence of angioinvasion .All the cases were associated with zygomycetes (mucormycosis)

Table 2:Classification of FRS in 65 cases

Classification of FRS	NO Of Patients	Immune Status	Fungal Identified
Fungal ball	46 (70%)	Immunocompetent(70%)	Aspergillus(50.%) Mucormycosis (15.4%) Asper & mucor (4.6%)
Chronic invasive fungal sinusitis	12 (18.4%)	Diabetes mellitus (9.2%) Immunocompetent(9.2%)	Mucormycosis (18.4%)
Chronic granulomatous FRS	1(2%)	Diabetes mellitus(2%)	Mucormycosis (2%)
Acute Fulminant FRS	6(9.2%)	Diabetes mellitus (9.2%)	Mucormycosis (9.2%)

Discussion:
In India, this disease was initially considered to be prevalent only in the northern regions, but is now reported from other parts of the country also.[7]

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).[13] However the diagnosis of fungal sinusitis depends on microscopical examination, culture and histopathology of tissue or the cheesy material obtained from sinuses. 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.[14]

Based upon histopathological findings, FRS is categorised as (1) non invasive FRS, which includes AFRS and Fungal ball and (2) Invasive FRS, which include chronic invasive FRS, chronic invasive granulomatous FRS and acute fulminant FRS.[8]

AFRS constitutes 5-10% of all cases of CRS.[9] These patients present with atopy, chronic intractable sinusitis with recurrent polyposis. Demonstration of fungal hyphae is important for diagnosis and diferentiating allergic mucin from a newly described entity eosiniphilic mucinous rhinosinisitis in which allergic mucin resembles AFRS but no fungus is demonstrated on histopathology or culture.[10,11]However in the present study none of the cases were diagnosed as AFRS. This is probably due to different climate and environmental factors.

In our study, Fungal ball was the most common type of FRS constituting 70% which was similar to Panda et al where in the incidence of fungal ball was 60%.[12] Patients with fungal ball present with nasal obstruction, chronic sinusitis. Diagnosing fungal ball/mycetoma is less challenging than other histologic categorjes of FS as fungal organisms were often abundant and easily seen on routine H&E stain. This can be mistaken for mucin or necrotic debri as they appear homogenous eosinophilic masses on low power examination So, higher magnification and Special stains such as GMS are required for confirmation. [6,8]mucormycosis and Aspergillus was the common fungal organism isolated in all the cases.

The chronic invasive FS (Granulomatous and Non Granulomatous) is characterised by hyphae actually within tissue, absence of fungal ball and presence of granulomatous inflammation.[15] Inflammatory exudates adherent to periphery of fungal ball should not be considered tissue invasion, some cases demonstrate splendore-Hoepelli phenomenon Which is one of the diagnostic clue to identify the fungus.

Acute Fulminant/ invasive Fungal sinusitis is a life threatening systemic illness largely attributed to mucormycosis in immunocompromised or diabetic patients.[8,16] In the current study, the commonly involved fungus was mucormycosis. The term Rhino-Orbito-Cerebral zygomycosis (ROCM) refers to the entire spectrum of disease which usually starts in the sinonasal tissue (limited sinonasal disease), progresses to the orbits (limited rhino-orbital disease) and finally affects central nervous system (rhino-cerebraldisease).[17] Similar presentation was seen in 2 cases of our study.

Acute fulminant FRS is characterised by necrosis, scant inflammation and vascular invasion. Pathological examination of peripheral areas sampled by surgeons is essential to assess adequacy of debridement.[18]

Management differs with the classification of fungal sinusitis. Acute fulminant FRS requires aggressive surgery and antifungal treatment. Chronic invasive/ granulomatous FRS requires surgical removal and antifungal therapy. Non invasive FRS(Fungal ball) requires surgery alone and allergic FRS requires steroids.

Conclusion
Though the clinical presentation and radiological findings may provide diagnostic clue for each fungal sinusitis category, histopathological examination and classification of FRS into invasive or non invasive disease is important with regards to treatment.

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