



ALLERGIC FUNGAL RHINOSINUSITIS: A CLINICO PATHOLOGICAL PROFILE

Dr. Saurabh Chawla	Assistant Professor
Dr. Jai Prakash Takkar	Assistant Professor
Dr. Nidhi Takkar*	Associate Professor *Corresponding Author
Dr. Shivika Mehta	Consultant

ABSTRACT

Background: Fungal rhinosinusitis presents as acute, chronic invasive and noninvasive based on duration and histopathologic evidence of fungal elements penetrating host tissue. Allergic fungal rhinosinusitis (AFRS) comes under non invasive group. AFRS is characterized by the formation of allergic mucin containing sparse fungal hyphae, numerous eosinophils and charcot-layden crystals. **Objective:** To correlate the presence of fungus in tissue with KOH, culture and analyze the clinical conditions associated with allergic fungal rhinosinusitis. **Methods:** Retrospective study was performed from November 2004 to November 2010 and prospective from December 2010 to November 2012 in a tertiary care centre. Clinically diagnosed cases of chronic rhinosinusitis with biopsy were selected for study. Relevant clinical details, histopathology and culture wherever done as documented in medical records were taken. **Results:** A total of 26 cases (40%) of allergic fungal rhinosinusitis were recorded out of 64 cases of fungal rhinosinusitis. Males and females contributing 13 cases each with mean age distribution of 43 years. Most of the cases presented with nasal obstruction, headache and nasal discharge. Culture was done in 12 cases and out of that 5 were positive for fungus. **Conclusion:** AFRS is a disease entity that commands a great deal of interest. Our study does reveal that the prevalence of AFRS in refractory chronic rhinosinusitis was the highest and in all these cases, aspergillus was the causative agent. There is a scope to extend this study in near future with the use of ancillary techniques along with novel concepts of detection of fungal hyphae like fluorescein-labeled chitinase staining technique can be used.

KEYWORDS : Allergic fungal rhinosinusitis, chronic rhinosinusitis, paranasal sinuses

INTRODUCTION

The term rhinosinusitis is commonly used rather than sinusitis as they share involvement in various inflammatory processes.¹ Rhinosinusitis (RS) is one of the most common health care problems across the world. Approximately 20% of people experience this disease in their life, chronic rhinosinusitis being the commonest and fungal accounting for 6-12% of rhinosinusitis causes.²

Plaignaud first reported fungal sinusitis in 1791 AD. Since then it has been an uphill task to diagnose this by clinicians because clinical picture is similar as bacterial sinusitis. Even radiological findings are non specific. That's why we have to rely on modalities like histopathology, culture and serology.^{3,4}

Fungal rhinosinusitis presents as acute, chronic invasive and noninvasive based on duration and histopathologic evidence of fungal elements penetrating host tissue. Allergic fungal rhinosinusitis (AFRS) comes under non invasive group.⁵

Allergic Fungal Rhinosinusitis (AFRS)

Allergic fungal rhinosinusitis is characterized by the formation of allergic mucin containing sparse fungal hyphae, numerous eosinophils and charcot-layden crystals.⁶

History : In 1976, Safirstein noted a combination of nasal polyposis, crust formation, and sinus cultures yielding *Aspergillus* species and observed its similarity with allergic bronchopulmonary aspergillosis (ABPA).^{4, 7} The term AFRS was introduced by Robson et al in 1989.⁸

Ferguson described a form of CRS histologically similar to AFS as described by DeShazo et al except for the absence of fungal hyphae, which she called eosinophilic mucin rhinosinusitis (EMRS).⁹

MATERIAL AND METHODS

The retrospective study was conducted from November 2004 to November 2010 and prospective study from December 2010 to November 2012 in a tertiary care centre. The cases of chronic rhinosinusitis investigated with biopsy were selected for study. Relevant clinical details of the patient including co-morbidities, histopathology reports and culture wherever done as documented in medical records were retrieved.

For prospective study, similar pattern was followed for the biopsies which we got from Department of ENT and referred cases from December 2010 to November 2012.

Histopathological examination of smears prepared from paraffin embedded tissues reviewed after staining with Hematoxylin & Eosin, Gomori's methenamine silver and Periodic Acid Schiff stains.

RESULTS

In our study a total of 64 cases of fungal rhinosinusitis identified out of 263 chronic rhinosinusitis cases, AFRS being the commonest with 26 accounting for 40% of FRS cases. Majority of patients presented with nasal obstruction, headache, nasal discharge and facial pain.

We saw a season trend in number of patients.

In the month of Jan-April total 08 patients of AFRS were reported, 12 in month of May-Aug and 06 in Sep-Dec month.

Table – 01 Culture & Histopathology

	Histopathology positive	Histopathology negative
Culture positive	02	03
Culture negative	03	04

Table 1 is depicting Culture and Histopathology comparison, where Culture and Histopathology was positive in 2 cases

(true positive), culture positivity and Histopathology negativity was seen in 03 cases (false positive), culture negativity and Histopathology positivity was seen in 3 cases (false negative) and in 04 cases was seen both culture and Histopathology negativity (true negativity). So discordance was noted in total of 6 cases.

Table – 02 Absolute Eosinophil Count (AEC) in AFRS Cases

AEC (cumm)	Number of patients(24)	Percentage
50-350	06	25
350-700	11	46
>700	07	29

Table 02 shows absolute eosinophil count for 24 of AFRS cases where it was done. Among them 6 cases had normal range of AEC where as 11 were in range of 350-700 and rest were more than 700/cumm. So majority were having high absolute eosinophil count.

Microphotograph

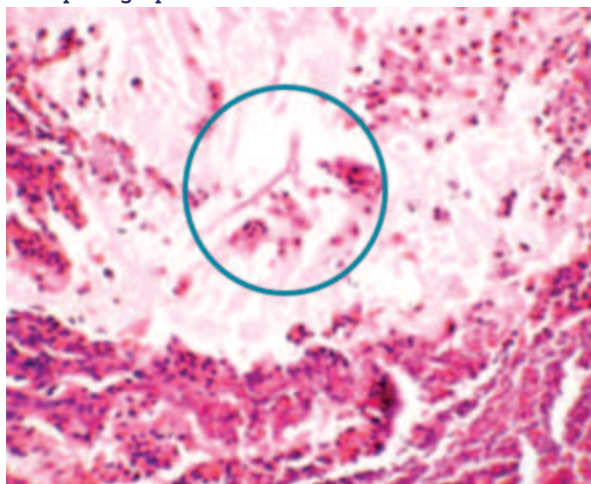


Fig1: Fungal hyphae (encircled) present in mucin pool and dense inflammatory cell infiltrate comprising of predominately eosinophils. (H&E, original magnification x 400)

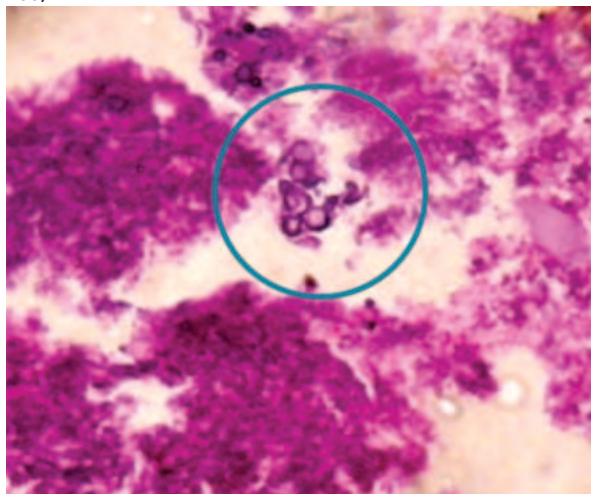


Fig 2: Allergic mucin with densely packed eosinophils and fungal organism (encircled). (H&E, original magnification x 400)

DISCUSSION

We conducted a combined retrospective and prospective study of eight year duration in our institute. A total of 263 cases of chronic rhinosinusitis investigated with biopsy were selected for study and of that fungal rhinosinusitis cases were 23.4%. Among these AFRS was the commonest entity accounting for 40% of FRS cases. These AFRS cases were

analyzed and correlated with clinical presentation, KOH, culture and biopsy.

Pathophysiology

Fungal allergens elicit immunoglobulin E (IgE)-mediated allergic and possibly type III (immune complex)-mediated mucosal inflammation in the absence of invasion in an atopic host.^{10,11} There occurs production of allergic mucin which present as plugs and cause fungal stasis with inflammatory response mediated by release of major basic protein, eosinophil peroxidase, eosinophil-derived neurotoxin, tumor necrosis factor β, and interleukins (IL)-4, 5, 10, and 13,39,40.¹²

For AFRS diagnosis, Bent and Kuhn proposed diagnostic criteria based on observations in 20 patients which include Type I hypersensitivity, nasal polyposis, characteristics CT scan findings, presence of eosinophilic mucus, positive fungal smear and few minor criterias like co-existence asthma, radiographic bone erosion, charcot Leyden crystals, serum eosinophilia etc.^{10,13}

Radiological Features

The demonstration of sinusitis on plain sinus roentgenograms in one or more paranasal sinuses is one of the diagnostic criteria for AAS. Haziness or clouding of the sinus or multiple sinuses is the most common feature. Characteristic feature on CT scan is the occurrence of heterogeneous densities, signifying opacification of the sinuses. Whereas on MRI, AFRS is characterized by areas of decreased T1 weighted signal intensities corresponding to the hyperattenuated lesions seen on CT.¹⁴

Urban and rural area sub categorization was done in which 80% of all FRS cases were from rural population. The reason for this age distribution and rural sector predominance could be again attributed to their field or other outside work. If we compare this parameter with Joshi et al, they observed more cases from urban population around 57% of cases.

There was present seasonal variation in our study with incidence showing fluctuations in each month but majority were in rainy season and summers (18 cases = 70%) compared to 30% cases in winters. This variation can be explained by humidity and high temperature during this period promoting fungal growth.

Among 26 AFRS cases, 06 patients had co morbidities, diabetes being the commonest in 2 cases. The ketone reductase system of fungi assists with adaptation to the environment and impairs the phagocytic function of polymorphonuclear leukocytes. Rest 2 cases had DNS and 1 case each with hypertension and history of nasal surgery.

Our patient of DNS encountering FRS can be explained by the use of long term antibiotics and antihistaminics. Patient with surgical history also received long term antibiotics.

Culture was done in 12 AFRS cases and it came out positive in 05 cases. Culture when compared with histopathology and was noted discrepancies between the two in 06 cases. Out of 06 cases, 03 were culture positive and histopathologically negative. As fungi are ubiquitous in nature^{8,10} and any environmental or commensal one can grow on media whenever suitable environment is there.

Other reason could be material which we received was scanty or from some different area as was sent for culture. Rest of 03 discordant cases which were histopathologically positive and culture negative can be explained by presence of abundant mucin. This mucin usually entraps the fungal hyphae and prevents them from reaching the surface, which gives a negative culture result. This can be overcome by use of mucolytic agents.

Absolute eosinophil count was calculated in 24 cases and majority of cases had raised count ie. more than 350/cumm.

CONCLUSION

Fungal rhinosinusitis once considered uncommon is seen quite frequently these days in unresponsive CRS cases. So we should keep this in mind in interpreting biopsies and histology is very important in subtyping of FRS and further planning management strategy.

AFRS is a disease entity that commands a great deal of interest. Our study does reveal that the prevalence of AFRS in refractory chronic rhinosinusitis was the highest and in all these cases, aspergillus was the causative agent. There is a scope to extend this study in near future with the use of ancillary techniques like PCR and In situ hybridization along with novel concepts of detection of fungal hyphae like fluorescein-labeled chitinase staining technique. can be used.

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