Original Article

Rhinosinusitis

# Allergic Fungal Rhinosinusitis: Microbiologic and Pathologic Review

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## ABSTRACT

**Objective:** To observe the various aspects of allergic fungal rhinosinusitis (AFRS).
**Study Design:** Prospective Study
**Place and Duration of Study:** This study was conducted at Department of Head and Neck Surgery, Civil Hospital Quetta and Chaudhary Rehmat Ali Memorial Trust Hospital, Lahore from 1st January 2015 to 30th June 2015.
**Materials and Methods:** Sixty seven patients suffering from chronic rhinosinusitis with polyps were included in this study. They were assessed clinically, computed tomography and histopathologic and mycologic monitoring. Depending on the presence or absence of allergic mucin and mycelial elements in the sinus, the patients were studied for different parameters.
**Results**: The mean age of 36.4 years with ranged from 14 to 51 and male to female ratio was 1.6:1. Out of these presumed 67 AFRS patients, 8 had positive fungal cultures. Remaining 59 patients with EM either had negative fungal cultures and these patients were thought to have insufficient evidence for a pathologic diagnosis of AFRS.
**Conclusion:** For the diagnosis of AFRS, the detection of fungal elements and allergic mucin should be considered.
**Key Words:** Allergic fungal, Chronic rhinosinusitis, Pathologic review

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## INTRODUCTION

Allergic fungal sinusitis (AFS) or rhinosinusitis (AFRS) is a form of polypoid chronic rhinosinusitis that is believed to be due to hypersensitivity to fungal antigens.[1,2] Allergic fungal rhinosinusitis (AFS) is thought to be a part of the disease spectrum of chronic rhinosinusitis, which affects between five to fifteen per cent of the population.[3] Allergic fungal sinusitis and eosinophilic mucin rhinosinusitis can easily be misdiagnosed and treated as chronic sinusitis, causing continuing harm.[4] Forms of chronic rhinosinusitis, such as allergic fungal rhinosinusitis (AFRS), could mimic malignant features.[5] Fungal rhino sinusitis (FRS) is an important infection of paranasal sinuses, which encompasses two main categories; invasive and noninvasive forms according to histopathological findings.[6] Fibroblasts are implicated in tissue remodeling and recruitment of inflammatory cells in chronic rhinosinusitis (CRS).[7]

Plonk and Luong[8] demonstrated that key role of cytokines imitative from respiratory epithelial cells, as well as interleukin (IL)-25, IL-33, and thymic stromal lymphopoietin, in the orchestration of both innate and adaptive T helper 2 immune responses that are vital components of the immunopathology of chronic rhinosinusitis with nasal polyposis and AFRS.[8] AFRS was seen to be more aggressive in children with increased fungal load when compared with adults.[9] Our understanding of the pathogenesis and treatment of allergic fungal rhinosinusitis (AFRS) continues to evolve.[10] The spectrum of fungal involvement in CRS runs from benign colonisation to potentially life-threatening invasive disease.[11]

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## MATERIALS AND METHODS

This prospective cross-sectional study was carried out at Department of Head and Neck Surgery, Civil Hospital Quetta and Chaudhary Rehmat Ali Memorial Trust Hospital, Lahore from 1st January 2015 to 30th June 2015. Sixty seven patients with CRS (of >3 months' duration) with nasal polyposis were included. Those patients who have apparent immune-compromised status or with histologic documentation of invasive fungal disease were not included. The detailed medical history along with clinical examination including preliminary nasal endoscopy was carried out in all patients. Aspirin sensitivity was assessed from history alone. Bronchial asthma was thought in those patients who were under the care of a pulmonologist and were on bronchodilator therapy. Patients were examined for follow-up during the study period. All patients underwent computed tomography (CT) of the paranasal sinuses and orbit in the axial and coronal planes, total leukocyte count, differential leukocyte count, absolute eosinophil count, and fasting blood sugar level estimation. All surgically/endoscopically

excised sinus mucosa and intrasinus debris were equally divided into two halves. One half was used for histopathologic monitoring, and the other half was used for mycologic examination. The histopathologic examination was carried out for the presence or absence of extramucosal allergic mucin, eosinophil clusters, Charcot-Leyden crystals, fungal hyphae, and possible mucosal invasion by fungal hyphae. The portion of surgically excised specimen used for mycologic examination was collected in sterile normal saline

# RESULTS

The mean age of the patients was 36.4 years ranged from 14 to 51 years with male to female ratio was 1.6:1 (Table 1). Positive culture test results indicate that age group up to 20 years is the most prone to AFRS (14.45%) whereas the age group above 40 years is the least affected. Average of patients that suffer from AFRS is 10.35%. AFRS was diagnosed in 8 patients. The diagnosis of AFRS was established using pathologic criteria by either the presence of eosinophilic mucin (EM) containing fungal forms on histologic examination using a GMS stain or the presence of EM without histologic evidence of fungi but with positive fungal cultures. Out of the presumed 67 AFRS patients, 8 had positive fungal cultures. The remaining 59 patients with EM either had negative fungal cultures and these patients were considered to have insufficient evidence for a pathologic diagnosis of AFRS (Table 2).

**Table No.1: Demographic statistics of the patients (n = 67)**

| Variable | No. | % |
|---|---|---|
| **Age (years)** | | |
| Upto 20 | 28 | 41.8 |
| 21- 40 | 22 | 32.8 |
| > 40 | 17 | 25.4 |
| **Gender** | | |
| Male | 40 | 59.7 |
| Female | 25 | 40.3 |

**Table No.2: Summary of culture test results**

| Age (years) | Samples tested | Positive culture | Negative culture |
|---|---|---|---|
| Upto 20 | 28 | 4 | 24 |
| 21- 40 | 22 | 3 | 19 |
| > 40 | 17 | 1 | 16 |
| Total | 67 | 8 | 59 |

# DISCUSSION

Allergic fungal rhinosinusitis (AFRS) is a type of chronic rhinosinusitis in which patients classically suffer from nasal polyps, type I IgE-mediated hypersensitivity, characteristic findings on computed tomography scans, eosinophilic mucin, and positive fungal stain.[12,13] Allergic fungal sinusitis (AFS), also referred to as allergic fungal rhinosinusitis (AFRS), is a noninvasive, eosinophilic form of recurrent chronic allergic hypertrophic rhinosinusitis.[14]

The interaction between fungi and the sinonasal tract results in a diverse range of diseases with an equally broad spectrum of clinical severity. These conditions may be discussed under two major headings: non-invasive disease (localized fungal colonization, fungal ball and allergic fungal rhinosinusitis) and invasive disease (acute invasive rhinosinusitis, chronic invasive rhinosinusitis and granulomatous invasive rhinosinusitis).[15] Aspergillus sp. or dematiaceous species were the most common fungi isolated in AFS while Aspergillus sp. was most common in FB and AIFRS.[16] In other studies Aspergillus ssp. were the most prevalent followed by Bipolaris sp. and Curvularia.[17] The presence of eosinophils in the allergic mucin, and not a type I hypersensitivity, is likely the common denominator in the pathophysiology of AFS.[18]

The presence of allergic mucin is not unique to allergic fungal sinusitis, but rather is the result of a process that could have other etiologies.[19] Local IgE specific for a range of antigens has been identified in sinus and inferior turbinate tissue in patients with allergic fungal rhinosinusitis.[20] The total IgE concentration was significantly lower in patients with fungal presence in sinuses. Multiple elevations of fungal IgE are adequate diagnostic evidence of these fungi when fungal cultures and histologic examinations are negative in diagnosing AFS.[21] Nasal polyps occurred more frequently in patients with fungal presence in sinuses.[22] In AFRS patients, fungal antigens stimulated T-cell activation, inducing a predominantly the immune response. Healthy controls expressed an inhibitory cytokine IL-10 when exposed to these fungal antigens, possibly serving as a protective response.[23]

Recent studies demonstrate a central role of cytokines derived from respiratory epithelial cells, including interleukin (IL)-25, IL-33, and thymic stromal lymphopoietin, in the orchestration of both innate and adaptive T helper 2 immune responses that are important components of the immunopathology of chronic rhinosinusitis with nasal polyposis and AFRS.[8] In AFRS and EMCRS patients, only fungal-specific CD4(+) T-cell proliferation occurred; hence, a lack of CD8(+) T-cell proliferation and activation in the presence of sinus eosinophilic mucus in these patients, regardless of fungal allergy, is a novel finding. This raises the question whether a dysfunctional CD8(+) T-cell response predisposes to ineffective clearance and accumulation of fungi in the sinuses of susceptible patients.[24]

Patients with AFS and HSD have HLA-DQB1 *03 alleles as a risk factor for disease, with AFS having the highest association.[25] Allergic fungal rhinosinusitis is a disease of young, immunocompetent individuals.[26] Demographic and socioeconomic factors may affect

AFRS presentation and treatment.[27] Proper diagnosis of AFS and differentiation from the other forms of both noninvasive and invasive fungal rhinosinusitis requires strict adherence to published diagnostic criteria.[28] Nasal obstruction, nasal discharge, nasal allergy and proptosis were the most common presentations.[29,30] Visual symptoms, proptosis, headaches, and increased nasal symptoms, especially in association with bony erosions on sinus computed tomography, suggest allergic fungal sinusitis and its complications in patients with chronic rhinosinusitis and nasal polyps. Patients with allergic fungal rhinosinusitis may present with a complication of the disease as the first symptom.[31]

The diagnosis of AFRS depends on history, the characteristics of CT scanning, pathology, mycologic and immunologic test.[32] The presence of more than one genotype in clinical samples illustrates the possibility that persons may be colonized by multiple genotypes and that any isolate from a clinical specimen is not necessarily the one actually causing infection.[33]

Acute invasive FRS showed unilateral pacifications of the sinonasal cavity, perisinus fat infiltration and/or bone destruction. Chronic invasive FRS demonstrated mass like hyper-attenuating soft tissue, with bony destruction. The soft tissue changes were hypointense on T1 and markedly hypointense on T2-weighted images. In allergic FRS, hyper-attenuating soft tissue causing paranasal expansion due to allergic mucin was observed on CT. Fungus ball presented as a hyper-attenuating lesion with calcifications within a single sinus.[34]

# CONCLUSION

Allergic fungal rhinosinusitis may be caused by variety of fungi, of which dematiaceous species is most common.

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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