



E-ISSN: 2706-9575  
P-ISSN: 2706-9567  
IJARM 2022; 4(1): 85-89  
Received: 07-11-2021  
Accepted: 09-12-2021

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## Diagnosis and management of allergic fungal sinusitis

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**DOI:** <https://doi.org/10.22271/27069567.2022.v4.i1b.341>

### Abstract

**Background:** Fungal Rhinosinusitis is one of the common diseases affecting the Nose and Paranasal Sinuses. Various fungi cause the disease. These infections are termed as invasive Fungal Infections, when they occur in immunologically compromised individuals, and Diabetics.

**Objective:** To evaluate the use of diagnostic criteria to confirm the fungal rhinosinusitis disease with radiological, pathological and microbiological investigations and their management.

**Materials and Methods:** A prospective observation study has been conducted at, in which 21 patients presenting to the Ear, Nose and Throat (ENT) department of our institution with clinical features of fungal sinusitis. After thorough clinical examination, the patients underwent investigations including hematological tests, radiological tests, diagnostic nasal endoscopy, histopathological examination and microbiological examination. Clinical examination including complete ENT & Head and Neck examination and cranial nerves examination was done to all the 21 patients included in the study. The data collected was imported into excel sheet (Microsoft Excel) for further evaluation in obtaining the results. The frequencies of distribution of various variables of the study were represented in the form of tables.

**Results:** 19 patients presented with nasal obstruction, 18 with nasal discharge, 14 with sneezing, 8 with headache, 11 with anosmia, 8 with nasal allergy, 9 with asthma, 7 with Diabetes mellitus, and 7 with previous history of nasal surgery. On clinical examination, polyps were found in 16 patients.

**Conclusion:** Post-operative use of Systemic and Local Steroids, Antihistamines, Decongestants, Regular nasal douching and Anti-fungal antibiotics wherever necessary, helps in early healing of the cavities and also reduces recurrence. Postoperative regular follow up for endoscopic suction clearance of the debris, crusts, and removal of granulation tissue, helps in identifying early recurrence and gives the surgeon to plan further treatment.

**Keywords:** fungal rhinosinusitis, nose and paranasal sinuses, coccidioidomycosis, mucor mycosis

### Introduction

Fungal Rhinosinusitis is one of the common diseases affecting the Nose and Paranasal Sinuses. Various fungi cause the disease. Although Fungal infections of man have been established as a distinct clinical entity since long time, the incidence of Fungal Rhinosinusitis is being published since 80's [1, 2]. Fungal Rhinosinusitis presents with variable clinical features in patients, depending upon the actual pathogenesis underlying the disease. It is being reported in large numbers in the recent times. Mucosal infiltration of the fungi resulting in a clinical entity finds the place in standard textbooks [3, 4, 5]. The common fungi that cause the disease are Aspergillus, Mucor mycosis, Curvalraia, Alternaria, Candidiasis, Coccidioidomycosis, Cryptococcosis, Actinomycosis, etc. These infections are termed as invasive Fungal Infections, when they occur in immunologically compromised individuals, and Diabetics. The clinical entity which occurs in immunocompetent individual with allergy to fungi, presents with polyps in the Nose and PNS is termed as Allergic Fungal Rhinosinusitis. This Atopic nature of the person who reacts immunologically to produce polyps in the presence of the fungi in the mucin. Allergic Fungal Rhinosinusitis (AFS) occurs in all parts of India [6, 7, 8]. Case reports recorded from all over the world, find the place in various journals include from India, Sudan & USA. Probably the disease might have existed even before 80s, but not recognized as a distinct clinical entity due to various reasons. Many of the cases treated previously, as Polyposis might be AFS in fact. Now that specific criteria are outlined to diagnose AFS clinically, Radiologically, Pathologically and Treatment protocols are prescribed, with FESS and Steroids [9, 10, 11].

AFS is being identified more frequently and being treated effectively. Present study is an attempt to review the Allergic Fungal Infections of Nose and PNS in the light of available latest concepts of Diagnosis and managing the disease.

### Materials and Methods

**Study design and setting:** This is a prospective observational study undertaken at.

**Study participants and sampling:** 21 patients presenting to the Ear, Nose and Throat (ENT) department of our institution with clinical features of Allergic Fungal Rhinosinusitis and willing to take part were included in the study. Those who are chronically ill and with other severe comorbidities were excluded from the study.

**Data collection procedures:** Clinical examination including complete ENT & Head and Neck examination and cranial nerves examination was done to all the 21 patients included in the study. After thorough clinical examination, the patients underwent investigations including hematological tests, radiological tests, diagnostic nasal endoscopy, histopathological examination and microbiological examination. Hematological tests included Absolute Eosinophilic Count (AEC), Hemoglobin percentage, Total White Blood Cell counts, Differential count, E.S.R, bleeding time, Clotting time, Platelet Count, R.B.S/F.B. S, Blood Urea, HBS Ag and HIV screening. Radiological tests included X-RAY (water's view), C.T SCAN PNS - Coronal & Sagittal section.

Histopathology examination (HPE) included HPE of Tissue obtained during Surgery, HPE of mucus & mucopus in OPD, and Special stains (Gomori Methanamine Stain). Microbiological tests included KOH Microscopy and Culture for Fungus. All the patients were managed medically by Preoperative intranasal steroids (Budesonide, Beclomethasone) and Preoperative oral steroids (Prednisolone for 3 - 4 weeks). Surgical management was Functional Endoscopic Sinus Surgery (FESS).

The patients were managed postoperatively by Postoperative intranasal steroids (Budesonide, Beclomethasone) for 6- 12 months, Postoperative systemic steroids (Prednisolone – tapering dose for 3 weeks and maintenance dose for 3 months) and Postoperative Antihistamines for 6-12 months.

The patients were followed twice weekly for first 2 weeks, once a week for next 2 weeks, once a month for 6 months and there after once in 6 months. Endoscopic suction clearance was done at each visit. All the clinical findings and investigative findings were recorded and significant findings were represented in the chart forms.

**Statistical analysis:** The data collected was imported into excel sheet (Microsoft Excel) for further evaluation in obtaining the results. The frequencies of distribution of various variables of the study were represented in the form of tables.

### Observation and Results

In this prospective study, 19 patients presented with nasal obstruction, 18 with nasal discharge, 14 with sneezing, 8 with headache, 11 with anosmia, 8 with nasal allergy, 9 with asthma, 7 with Diabetes mellitus, and 7 with previous history of nasal surgery. (Table 1) On clinical examination, polyps were found in 16 patients. Thick mucus or mucopus secretions were seen in 19 patients, sinus tenderness in 6 patients. (Table 2) Hyperglycemia was seen in 7 patients and AEC raised (> 500/ c.mm) in 6 patients only. All patients were screened for HIV and HBS Ag and found non-reactive. Radiological study of the PNS done by X-Ray and CT scan. In all cases, X-Rays showed haziness (ground glass appearance) of maxillary and ethmoid sinuses. CT scan PNS showed altered density of maxillary sinuses in 16 patients. DNE was done for all cases. 16 patients were found to have polyps and 19 patients with thick mucus / mucopus. The secretions were taken for KOH microscopic study and culture. In the present study, branched septate mycelium, suggesting Aspergillus was seen in samples of 13 patients. (Table 3) 8 patients received preoperative intranasal steroids like Budesonide and Beclomethasone and 11 patients received preoperative oral steroids (Prednisolone). Of 21 patients, all underwent FESS for removal of diseased sinuses in total. Post operatively, all patients received intranasal steroids and systemic steroids. In present study, Aspergillus was the commonest organism identified in 13 patients, Alternaria in 1, and Culveria in 2 patients from culture. (Table 4) Post operatively patients were given intranasal steroids and oral steroids. Oral steroids (prednisolone) were given for 3 weeks in tapering dose and maintenance dose (5mg) was given for 3 months. Intranasal steroids were given for a long period of 6 months to 1 year. Post operatively Anti-fungal treatment was given to 3 patients.

**Table 1:** Showing categorization of patients based on their clinical features

Clinical feature	Number of patients
Nasal obstruction	19
Nasal discharge	18
Sneezing	14
Anosmia	11
Headache	8
Nasal Allergy	8

Nasal obstruction was the commonest clinical feature followed by Nasal obstruction, Sneezing and Anosmia

**Table 2:** Showing categorization of patients based on their clinical examination findings

Clinical finding	Number of patients
Thick mucus or mucopus secretions	19
Polyps	16
Sinus tenderness	6

Thick mucus or Mucopus secretions were the most common clinical examination findings followed by Polyps and Sinus tenderness

**Table 3:** Showing categorization of patients based on their investigative (hematological, radiological and microbiological findings)

Investigative findings	Number of patients
Hyperglycemia	7
AEC raised (> 500/ c.mm)	6
X-Rays showed haziness (ground glass appearance) of maxillary and ethmoid sinuses.	21
CT scan PNS showed altered density of maxillary sinuses	16
Polyps on DNE	16
Thick mucus/mucopus on DNE	19
Branched septate mycelium, suggesting Aspergillus on KOH microscopy and culture	13

X-Rays showed haziness of maxillary and ethmoidal sinus in all 21 patients and Thick mucus/mucopus was commonest finding on DNE

**Table 4:** Showing categorization of patients based on their culture findings

Organism	Number of patients
Aspergillus	13
Culveria	2
Alternaria	1

Aspergillus was the commonest organism found on the culture, followed by Culveria and Alternaria

**Discussion**

Invasive Fungal Rhinosinusitis is commonly seen in uncontrolled diabetics<sup>[12, 13]</sup>, and other immunocompromised hosts like Transplantees, long term steroid users, certain malignancies especially hematological and AIDS patients. The true incidence of Allergic Fungal Rhinosinusitis among patients with sinonasal polyposis and chronic Rhinosinusitis remains unknown<sup>[14, 15]</sup>. The basic etiopathogenesis underlying Allergic Fungal Rhinosinusitis is unclear since the presence of fungus in the diseased sinonasal mucosa has not been confirmed to be pathogenic or just normal habitant flora.<sup>[16, 17, 18]</sup> Ponikau, *et al.*,<sup>[19]</sup> identified fungus in the nasal lavage from all 14 healthy control subjects in their study, demonstrating the ubiquitous nature of the fungus, thus questioning their pathogenicity. Out of 21 patients studied, 14 (66.6%) were male patients and 7 (33.3%) were female. The sex ratio is 2:1. John E. Mc Clay *et al.*,<sup>[20, 21]</sup> identified the disease pattern in male / female ratio in children is 2.1: 1 (average age 13 years) and in adults females dominated (M/F 1:1.4). Interestingly when the 2 groups of patients taken into consideration, the M/F ratio is 1.4: 1 (13-15 years)<sup>[22, 23]</sup>. In this study 90.4% patients (19) presented with nasal obstruction, 85.7% patients (18) presented with nasal discharge, 66.6% patients (14) with sneezing, 38% patients (8) with headache, 52.3% patients (11) with anosmia, 38% patients (8) with nasal allergy, 42.8% patients (9) with asthma, 33.3% patients (7) with Diabetes mellitus, and 33.3% patients (7) with previous history of nasal surgery. E. Serrano *et al.*,<sup>[22]</sup> reported in their study; previous history of asthma in 40-80% of cases and an atopic predisposition in 40-80% of patients<sup>[17, 19, 23, 24]</sup>. On clinical examination, polyps were found in 76.2% patients (16) of AFS. E. Serrano *et al.*,<sup>[22]</sup> reported in their study that nasal polyposis is seen in 90-100% of cases of AFS, Berrylin J Ferguson<sup>[13]</sup> stated that nasal polyps is seen in 90% of patients of AFS. Thick mucus or mucopus secretions were seen in 90.4% patients (19), Sinus tenderness in 31.5% patients (6). In this study hematological investigations including Hb%, TC, DC, ESR, BT, CT, Platelet count, RBS/FBS, Blood urea, Serum creatinine,

HIV, HBS Ag, Absolute Eosinophil count (AEC) were done for all patients. AEC is raised (> 500/ c.mm) in 31.5% patients (6) only. A. Ravi Kumar *et al.*,<sup>[18]</sup> stated that AEC is raised in 60% of patients suffering from AFS<sup>[14, 25]</sup>. Radiological study of the PNS done by X-Ray and CT scan. In all cases, X-Rays showed haziness (ground glass appearance) of maxillary and ethmoid sinuses. CT scan PNS showed altered density of maxillary sinuses in 76.2% patients (16) suffering from AFS. John E. McClay<sup>[20, 21]</sup> in his study of 140 cases noted typical heterogeneous opacification and almost uniform expansion of the affected sinuses. NO bony destruction was observed giving an impression of noninvasive nature. DNE was done for all cases. 84.2% patients (16) of AFS presented with polyps, 89.4% patients (17) with thick mucus / mucopus. The secretions were taken for study with KOH microscopy and for culture. In this study, unilateral involvement of the sinuses was seen in 38% (8) patients, bilateral involvement of the sinuses was seen in 62% (13) patients, one sinus was affected in 9.5% (2) patients. E. Serrano<sup>[22]</sup> stated that, unilateral pathology was seen in 35.2% and bilateral in 64.8%, one sinus was effected in 30.3% cases. John E. Mc Clay<sup>[20, 21]</sup> reported that, 49% of cases had unilateral, 51% bilateral disease. He also found that, unilateral involvement is more common in children than adults (70% vs 37%). 42.1% patients (8) of AFS received preoperative intranasal steroids like Budesonide, and Beclomethasone for a period of 3 weeks. 57.8% patients (11) received pre-operative oral steroids (prednisolone) initially 30mgs for 5days, followed by 20 mgs for 5 days, later 10mgms for 5days. 94.7% patients (18) of AFS underwent FESS. 94.7% patients (18) received postoperative intranasal steroids (Budesonide) and 88.2% patients (15) received postoperative systemic steroids (Oral Prednisolone). In the Diagnosis of Fungal Rhinosinusitis, the Microbiologist and Pathologist have a very significant role to play, as identification of fungal elements in the mucin is one of the diagnostic criteria for AFS. Similarly, identification of fungal elements in the submucoasal layers in HPE indicates invasive nature of the disease. Culture for Fungus was positive in 76.2% (16 of total 21 patients). Aspergillus was the commonest organism identified in 81.2% patients (13) of this study, Alternaria was in 6.2% patients (1), and Curvularia in 12.5% patients (2). Mark stated Bipolaris speciferaand Curvularia lunata are most common causative fungi reported overall.<sup>[26]</sup> V. Rupa *et al.*,<sup>[27]</sup> reported that fungal culture was positive in 96% of cases and the most common fungal isolate was Aspergillus (92%, 23 of 25cases)<sup>[19, 25, 28]</sup>. In the present study, it was found that the direct smear examination with KOH was more informative and specific. Branched septate mycelium suggesting Aspergillus was found in 68.4% (13) of AFS cases

HPE is the only confirmatory evidence to classify fungal sinusitis into Invasive and Non-invasive types. All the cases showed the histopathological criteria required for the diagnosis of AFS, that is the allergic mucin is characteristic in HPE, which shows onion layered pattern, pale eosinophilic back ground with large pyknotic eosinophilic concretions and also shows Charcot layden crystals, basophils and occasional fungal elements. Methenamine silver stain of Allergic mucin is positive for fungal hyphae, but no fungal hyphae are seen in the mucosa.

Sinus mucosal H&E stain of AFS characteristically shows mucosal infiltrate of eosinophils, plasma cells and small lymphocytes. Absence of necrosis, granuloma formation, giant cells, stromal edema and thickened epithelial basement membrane are also seen. Other features like partially desquamated epithelium and distended mucus glands are present in HPE [14, 17, 19, 20, 22]. Polyps showed inflammatory features.

Post operatively patients of AFS were given intranasal steroids and oral steroids. Oral steroids (prednisolone) were given for 3 weeks in tapering dose and maintenance dose (5mg) was given for 3 months. Oral prednisolone was given only for 3 weeks in tapering dose without maintenance dose for 5 diabetics patients. Intranasal steroids and antihistamines were given for a long period of 6 months to 1 year. Post operatively patients were followed twice weekly for first 2 weeks, weekly for next 1 month, monthly for next 6 months. At each visit Endoscopic suction clearance was done Post operatively Anti-fungal agents Itraconazole 200mgs for a period of 3 months was given in 100% patients of AFS where the HPE was doubtful in regards with invasion. Topical Amphotericin effective in preventing recurrence [31].

In this study, out of all patients with Allergic fungal sinusitis, it was found that 15.7% patients (3) had early recurrence, 15.7% patients (3) had delayed recurrence. and 66.6% (14) of total 21 cases had no recurrence. Schubert and Goetz [15, 29] reported the long-term clinical outcome of 67 patients following initial surgical therapy of AFS. Patients treated with 2 months of oral corticosteroids were significantly less likely to have experienced recurrent AFS (35%) than those who had not (55%) [13, 20].

### Conclusion

Allergic Fungal Rhinosinusitis is one of the common clinical entity encountered in the ENT practice. The incidence of the disease is increased tremendously in the past two decades because of increased Atopic nature in the present highly polluted environment, increased incidence of comorbid illness like diabetes mellitus, other chronic illness and definitely increased availability if investigative techniques. Post-operative use of Systemic and Local Steroids, Antihistamines, Decongestants, Regular nasal douching and Anti-fungal antibiotics wherever necessary, helps in early healing of the cavities and also reduces recurrence. Postoperative regular follow up for endoscopic suction clearance of the debris, crusts, and removal of granulation tissue, helps in identifying early recurrence and gives the surgeon to plan further treatment.

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