

DIAGNOSIS & MANAGEMENT OF ALLERGIC FUNGAL SINUSITIS

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ABSTRACT

BACKGROUND

Chronic sinusitis is one of the common diagnosis in ENT practice. Allergic fungal sinusitis is a clinical entity with characteristic clinical, radiographic and histopathological findings. Allergic fungal sinusitis and eosinophilic mucin rhinosinusitis can easily be misdiagnosed.

AIM OF STUDY

A prospective clinical study of allergic Fungal Rhinosinusitis to use diagnostic criteria to confirm the disease with Radiological, Pathological & Microbiological investigations and their management.

MATERIALS & METHODS

A prospective study of allergic Fungal Rhinosinusitis in 2 years from November 2011 to October 2013. Among the patients who attended the ENT OPD during this period, 21 patients with symptoms and signs suggestive of Allergic Fungal Rhinosinusitis are selected.

KEYWORDS

Allergic Fungal Sinusitis, Aspergillus, Rhinosinusitis, Curvularia.

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INTRODUCTION: Fungal Rhinosinusitis is one of the common diseases affecting the Nose and Paranasal Sinuses. Various fungi cause the disease. Mucosal infiltration of the fungi resulting in a clinical entity finds the place in standard textbooks. The common fungi that cause the disease are Aspergillus, Curvularia, Alternaria, Candidiasis, Mucormycosis, Coccidioidomycosis, Cryptococcosis, Actinomycosis, etc. 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 (AFRS) occurs in all parts of India; case reports recorded from all over the world. Probably the disease might have existed even before 80s, but not recognised 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 is outlined to diagnose AFS Clinically, Radiologically, Pathologically and Treatment protocols are prescribed, with FESS and Steroids; 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 duration: Prospective hospital based interventional study between November 2011 to October 2013.

METHODOLOGY: All the 21 patients were subjected to clinical examination, and investigated by the following methods.

1. **Haematological:** Absolute Eosinophil count, Haemoglobin percentage, Total WBC counts, Differential count, ESR, Bleeding time, Clotting time, Platelet Count, Random Blood sugar/Fasting Blood sugar, Blood Urea, HBsAg, HIV were done for all patients.
2. **Radiological:**
 - X-RAY (Water's view).
 - CT SCAN PNS -Coronal & Sagittal sections.
3. **Diagnostic Nasal Endoscopy:**
4. **Histopathology:**
 - HPE of Tissue obtained during Surgery.
 - HPE of mucus & mucopus in outpatient department.
 - Special stains (Gomori Methenamine Stain).
5. **Microbiology:**
 - KOH Microscopy.
 - Culture for Fungus.

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MANAGEMENT:**Medical Line of Treatment:**

- Preoperative intranasal steroids (Budesonide, Beclomethasone).
- Preoperative oral steroids (Prednisolone for 3-4 weeks).

Surgery: FESS (Functional Endoscopic Sinus Surgery)**Postoperatively:**

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

Followup: Patients were followed twice weekly for first 2 weeks, once a week for next 2 weeks, once a month for 6 months and thereafter once in 6 months. At each visit, endoscopic suction clearance was done.

OBSERVATION: 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.

On clinical examination, polyps were found in 16 patients. Thick mucus or mucopus secretions were seen in 19 patients, sinus tenderness in 6 patients.

Hyperglycaemia was seen in 7 patients and AEC raised (>500/c.mm) in 6 patients only. All patients were screened for HIV and HBsAg and found nonreactive.

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 of the fungal mucin of KOH microscopy.

In this study, 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 toto. Postoperatively, all patients received intranasal steroids and systemic steroids.

In present study, *Aspergillus* was the commonest organism identified in 13 patients, *Alternaria* in 1, and *Curvularia* in 2 patients from culture.

Postoperatively, patients were given intranasal steroids and oral steroids. Oral steroids (prednisolone) were given for 3 weeks in tapering dose and maintenance dose (5 mg) was given for 3 months. Intranasal steroids were given for

a long period of 6 months to 1 year. Postoperatively, Antifungal treatment was given to 3 patients.

DISCUSSION: 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 80s. 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.

The present study is an attempt to review the application of required diagnostic criteria used by various authors, correlate the Radiological features with the clinical signs and Per-operative findings. Nasal smears, Nasal swabs, and Tissue collected during the surgery were subjected to Laboratory study to arrive at diagnosis. An attempt was also made to study the role of various treatment modalities used in the course of management of the diseases.

Invasive Fungal Rhinosinusitis is commonly seen in uncontrolled diabetics¹ and other immunocompromised hosts like Transplantees, long term steroid users, certain malignancies especially haematological and AIDS patients.

The true incidence of Allergic Fungal Rhinosinusitis among patients with sinonasal polyposis and chronic Rhinosinusitis remains unknown². The basic aetiopathogenesis 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.^{2,3,4}

Ponikau, et al.,⁵ 19 identified fungus in the nasal lavage from all⁵ healthy control subjects in their study, demonstrating the ubiquitous nature of the fungus, thus questioning their pathogenicity. They demonstrated characteristic allergic mucin histologically in 96% of their 101 cases, emphasising the importance of histopathological diagnosis for confirmation of AFS postoperatively.

A total number of 21 cases with features of Allergic Fungal Rhinosinusitis were taken during a period of 2 years for this study.

In this study, the youngest patient is 11 years old and the eldest is of 55 years old. The highest incidence was seen in the age group of 31-40 years, which was 9 in number (42.8%). 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. McClay et al.,⁴ 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 were taken into consideration, the M/F ratio is 1.4: 1 (13-15 years).^{6,7}

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.,⁶ reported in their study; previous history of asthma in 40-80% of cases and an atopic predisposition in 40-80% of patients.^{1,3,6,7,8}

On clinical examination, polyps were found in 76.2% patients (16) of AFS. E. Serrano et al.,⁶ reported in their study that nasal polyposis is seen in 90-100% of cases of AFS. Thick mucus or mucopus secretions were seen in 90.4% patients (19), Sinus tenderness in 31.5% patients (6).

In this study haematological investigations including Hb%, TC, DC, ESR, BT, CT, Platelet count, RBS/FBS, Blood urea, Serum creatinine, HIV, HBsAg, 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.,² stated that AEC is raised in 60% of patients suffering from AFS^{5,9}.

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.⁴ 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 effected in 9.5% (2) patients. E. Serrano⁶ stated that unilateral pathology was seen in 35.2% and bilateral in 64.8%, one sinus was effected in 30.3% cases. John E. McClay⁴ 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 preoperative oral steroids (prednisolone) initially 30 mg for 5 days, followed by 20 mg for 5 days, later 10 mg for 5 days. 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 submucosal 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 specifera* and *Curvularia lunata* are most

common causative fungi reported overall.¹⁰ V. Rupa et al.,¹¹ reported that fungal culture was positive in 96% of cases and the most common fungal isolate was *Aspergillus* (92%, 23 of 25 cases).^{3,9,12}

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-Leyden 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 oedema and thickened epithelial basement membrane are also seen. Other features like partially desquamated epithelium and distended mucus glands are present in HPE.^{1,3,4,5,6} 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 (5 mg) 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.^{4,13,14} Post operatively Antifungal agents Itraconazole 200 mg 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.

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 Goetz¹³ 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%).

CONCLUSION: Allergic Fungal Rhinosinusitis is one of the common clinical entity encountered in the ENT practice. The incidence of the disease has 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 illnesses and definitely increased availability of investigative techniques. The invasive nature of the disease has increased due to increased incidence of immunocompromised states like HIV infection, chemotherapy for various haematological malignancies like lymphomas and leukaemias.

Diagnosis predominantly based on the clinical presentation like Nasal Obstruction, recurrent URTI [upper respiratory tract infections], recurrent sneezes, rhinorrhoea, headaches, usually in the background of family history of Asthma and Nasal allergy.

Demonstration of fungal elements in the nasal smears on wet KOH preparations along with Allergic mucin and Eosinophils usually confirms the diagnosis of fungal sinusitis. culture and subtyping of the fungus along with histopathological confirmation of invasiveness will definitely changes the postoperative treatment as highlighted in the present study.

Presence of hyperinflamed allergic mucosa with impaired ciliary motility and obstruction of OMC [ostioameatal complex] results in accumulation of thick allergic mucin along with fungal spores which again initiates a vicious cycle popularly known as "AFS sinusitis cycle" term given by Mark S. Schubert. Presence of many anatomical abnormalities like Deviated Nasal Septum with or without spur, pneumatized middle turbinate [concha bullosa] and narrow Ostioameatal Complex which are better appreciated in DNE and CT scan will accentuate the problem.

Preoperative use of Steroids in the form of topical steroid sprays and oral preparations for a period of minimum four weeks has an added advantage of decreased the tissue oedema, bulk of polypoidal mass both of which helped in reducing bleeding during surgery and overall duration of the surgery as evident in the present study. It also gives symptomatic relief before surgery.

Endoscopic Sinus Surgery is useful in all the cases of Fungal Infections to clear the disease meticulously, improving the ventilation and drainage of the sinuses without disturbing the important Anatomical structures. Though majority of cases in this study were done under Local Anaesthesia, Hypotensive Anaesthesia helps in better clearance of the disease, and blood loss would be minimal. Postoperative use of Systemic and Local Steroids, Antihistamines, Decongestants, Regular nasal douching and Antifungal antibiotics wherever necessary, helps in early healing of the cavities and also reduces recurrence. Postoperative regular followup 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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