

Fungal Diseases of Nose and Paranasal Sinuses in a Rural Tertiary Care Hospital

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Abstract

Introduction: Fungi are ubiquitous in nature, and we are showered with their spores daily. In the recent past, the fungal infection has been increasing both as imported ills due to greatly enhanced international traffic and as opportunistic infection in consequence of the use of powerful cytotoxic drugs, steroids, and antibiotic therapy. Incidence of infection and death due to fungi has been grossly underestimated.

Materials and Methods: A total of 50 patients of Government Theni Medical College, Theni, who had clinical features suggestive of fungal infections of nose and paranasal sinuses were evaluated with standard pro forma-hematological investigations, radiological procedures, immunological procedures, and pathological diagnostics formed part of the armamentarium. Surgical management and follow-up were done.

Results: Out of 50 patients, 18 were male and 32 were female prominent age group being 21-40 all the patients had nasal symptoms and most of them headache. Nasal polyps and fungal mass were seen in all the patients. *Aspergillus flavus* constituted 40%, *Aspergillus fumigatus* and *Niger* accounted for 25%. Bilateral disease and involvement of ethmoidal sinus were noted in the majority of cases. Recurrence was observed in 6 of the cases, and orbital complications were observed in 8 of the cases.

Conclusion: About 100% of our series of 50 cases were histopathologically proven to be allergic *Aspergillus sinusitis*. CT was found to be highly effective for pre-operative evaluation and intraoperative guidance. Nasal polyposis was a concomitant feature in fungal sinusitis.

Key words: Allergic fungal rhinosinusitis, *Aspergillus*, Endoscopic sinus surgery, Fungal culture, Sinonasal polyposis

INTRODUCTION

Fungi are ubiquitous in nature, and we are showered with their spores daily. Fungal infections of nose and paranasal sinus are not common in man in industrialized countries. However, in the recent past, the fungal infection has been increasing as imported ills due to greatly enhanced international traffic and as opportunistic infections in consequence of use of powerful cytotoxic drugs (as applied to the treatment of neoplasm) and also steroids and antibiotic therapy.¹⁻³

The most common site of fungal infection in man is the lungs with or without hematogenous spread to other organs. However, the localized fungal infection can also occur in the upper respiratory tract and is more common than was previously suspected.^{4,6}

Most fungal species which are pathogenic to human cause opportunistic infection and only dermatophytes are transmissible from host to host. The incidence of infections and death due to fungi has been grossly underestimated moreover the list of fungal species capable of producing disease in immune compromised person is increasing rapidly.

In an era with AIDS, broad spectrum of antibiotics, cytotoxic drugs and the organ transplantation, fungal infection which affect the nose and the sinus are candidiasis, rhinosporidiosis.

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Aspergillus, phycomycosis, actinomycosis, coccidioidomycosis, histoplasmosis, cryptococcosis, blastomycosis, sporotrichosis, and nocardiosis.

Martin and Berson noted a high incidence in South Africa which they attributed particularly to malnutrition the largest series of case involve.⁷⁻⁹

In our study, the fungal infections mainly presented with nasal polyps, nasal block, nasal discharge, headache, and proptosis mimicking benign or malignant tumors of the nose and paranasal sinuses.

The warm moist climate in Kerala, coastal regions of Tamil Nadu and Andhra Pradesh with its attendant high rate of allergic, hypertrophic, vasomotor rhinitis, and rhinosinusitis provide one of the prerequisites for fungal infection of upper respiratory tract. The agricultural economy of these three states also accounts for the high prevalence of the fungal infections.

Of the fungal infections of nose and paranasal sinuses, aspergillosis tops the list in terms of occurrence.

Here, the ENT Department, Government Theni Medical College Hospital with its advanced facilities serves as a referral center provides various possibilities for carrying out a study in fungal infections focusing mainly on opportunistic infections of the nose and paranasal sinuses. The lack of recognition of this disease and the scarcity of the reports prompted us to undertake the study.

MATERIALS AND METHODS

The materials for this study were collected from patients who attended the outpatient Department of Government Theni Medical College Hospital between 2014 and 2016.

A total of 50 patients who had clinical features suggestive of fungal infection of nose and paranasal sinus were evaluated using a standard pro forma and underwent the following investigate procedures systematically as and when needed.

Hematological Investigations

Complete hemogram, blood sugar level, serum electrolyte, serum protein, blood grouping, etc., were done as preliminary investigations to assess the general health condition as well as to rule out any underlying disorders.

Radiological Procedure

Relevant X-ray of the nose and paranasal sinuses was taken for all patient and those who were provisionally diagnosed as fungal granulomas were subjected to CT scanning

of the nose, paranasal sinuses, and brain with contrast enhancement studies.

Immunological Procedure

Cutaneous reactivity to *Aspergillus* species was tested by the prick test.

Pathological Procedure

Biopsied material was placed in three sterile bottles as follow:

Bottle A containing sterile normal saline for staining with 10% potassium hydroxide bottle B with sterile normal saline for fungal culture.

Bottle A and B were transported to the microbiology lab within 1 h of the procedure.

Bottle C sent to the pathology department of histopathological examination.

Bottle A specimen was mounted with 10% potassium hydroxide. This dissolves or makes the tissue element translucent, and the fungi are easily observed when examined as wet preparation fungal elements stained black, easily visible.

Bottle B specimen was sent for fungal culture. It was cultured on potato - dextrose sugar. The best grade of white potatoes should be used. They should be washed and sliced, unpeeled at the rate 250 g/l of water and allowed to steam for 1 h in an autoclave with its exhaust open. The filtrate should be distinctly turbid. A clear filtrate is to be avoided agar and dextrose once added give serial concentration of 2% each and the whole was then tubed, autoclaved and stained for use. Properly made, each tube showed have a small button of sedimented material is its base. Potato-dextrose agar made in this manner in an excellent medium, this interval can sometimes be hastened by reducing the concentration of dextrose to 1%.

When growth was present, a bit of growth was removed from the colony, toasted apart in a drop of water and examined as a wet preparation.

Slide cultures show the structure and arrangement of the growth and true morphology and hence used.

These cultures were prepared by adding a bit of growth to a small portion of agar on a slide. A coverslip was placed on top and the slide was incubated in a moist Petri dish. After a week, when the spores had matured, the coverslip and medium were slowly removed. A drop of 10% KOH was added, and the coverslip replaced. Slide is heated gently and allowed to cool approximately 15 min. The preparation was then examined under microscope.

Some of the mycelium would have adhered to the slide and the spore head, conidiophores, etc., will be intact and seen in their characteristic arrangement. *Aspergillus* species was easily identified by the presence typical conidiophores.

Bottle C was used for routine histopathological examination of the specimen under low and high power magnification with a light microscope.

Our Treatment Policy

The adequate management of fungal infections of the nose and sinuses at our institute revolves around five major principles.

- a. Timely diagnosis, usually dependent on a high index of suspicion.
- b. Control of local and systemic predisposing factors.
- c. Surgical debridement geared to level of invasiveness of the fungus.
- d. Antifungal treatment.
- e. Long-term follow-up.
- f. All the patients in this study underwent.

Endoscopic Sinus Surgery

Postoperatively patients were advised to come for regular follow-up. The nasal douching was given to every patient for the 5th post-operative day after the first post-operative endoscopic examination and cleaning. Patient was treated by beclometasone aqueous nasal spray, antihistamine, and vitamins.

The patients were requested to come for follow-up on the 15th post-operative day for endoscopic examination and cleaning and whenever possible thereafter (usually once in a month). The patient with allergic *Aspergillus sinusitis* did not require antifungal therapy. Antifungal therapy was given based on the type of fungal infection and its invasiveness (mucormycosis).

RESULTS

All patients were evaluated as per the following parameter

1. Age
2. Sex
3. Clinical symptoms
4. Clinical sign
5. Histopathological examination
6. CT scan of nose and sinuses
7. Surgical procedure
8. Complications
9. Follow-up and recurrence.

The majority of cases were in 2nd group, is between 21 and 40 years (Table 1).

Out of 50 patients study, 18 were male and 32 were female. All of them were racially Indians.

There were more female than male in this study (Table 2). Females in this study formed 64% of total number of cases.

All patients, in our study, have nasal symptoms (100%). They are nasal obstruction, nasal discharge, postnasal discharge, frequent sneezing, reduced sense of smell (hyposmia) or complete loss of smell (anosmia), and nasal bleeding.

Ocular symptoms such as proptosis, epiphora, diplopia blurring of vision in our study were 16%.

Fungal culture, in our study, showed out of 50 patients. 20 are *Aspergillus flavus*, 8 *Aspergillus fumigates*, 4 are *Aspergillus niger*, 2 are *Aspergillus terreus* (Table 8).

DISCUSSION

The fungal diseases of the nose and paranasal sinuses encompass not one disease entity but a multitude of an entire spectrum of different diseases. We have studied different disease causes, namely allergic *A. sinusitis* (50 cases). Although the treatment of these diseases is vastly different, the presentation and clinical features are quite similar and thus they could be studied together. The authors have attempted to study these diseases under the common heading highlighting the important difference whenever required.¹⁰⁻¹²

AGE: The majority of cases in our study were between the age group of 21-40 years.

They constitute 68% of a total number of cases. This was followed by the age group between 41 and 60 years and <20 years who constitute 32% total number of cases.

This compares favorably with these studies.

Sex: In our study, there was a clear female preponderance numbering 32 out of 50 cases (64%) and male 18 out of 50 (36%) reported data by Waman *et al.* showed female preponderance with allergic *A. sinusitis* in our study was 64% female ratio (Table 3). This corresponds well with the previously mentioned study.

Symptoms: All patients in our study had nasal symptoms. The nasal symptoms included nasal obstructions, nasal discharge frequent sneezing, reduced smell (hyposmia) complete loss of smell (anosmia), and nasal bleeding. The next most common symptom was a headache was seen in 76% of our patient. The next most common symptoms

Table 1: Age n=50

Age	Number of patient (%)
<20	8 (16)
21-40	34 (68)
41-60	8 (16)
>60	-

Table 2: Sex n=50

Total number of cases	Males	Females
50	18	32

Table 3: Age/sex/incidence n=50

Age	Sex		Incidence		Total
	Male	Female	Male (%)	Female (%)	
<20	2	6	4	12	16
21-40	12	22	24	44	68
41-60	4	4	8	8	16
>60	-	-	-	-	-

Table 4: Clinical symptoms n=50

Symptoms	Number of patients (%)
1. Nasal Nasal obstruction Nasal discharge Post nasal Discharge	50 (100)
2. Headache	38 (76)
3. Ocular	8 (16)

Table 5: Clinical signs n=50

Sign	Number of patient (%)
1. Nasal polyp and fungalmass	50 (100)
2. Ocular manifestations Proptosis Epiphora Diplopia Ophthalmoplegia	8 (16)

were ocular symptoms such as epiphora, diplopia and blurring of vision comprising about 16% (Table 4).^{13,14}

Various other studies showed that the common symptoms in allergic *A. sinusitis* are chronic nasal obstruction and postnasal discharge. These findings compare favorably with our studies.

Signs: In our study, out of 50 patients, all 50 patients presented with nasal polyps, fungal mass (100%). The ocular sign such as proptosis diplopia and ophthalmoplegia was seen 16% (Table 5).

Table 6: Histopathology and fungal culture n=50

Causative organism	Number of patient (%)
<i>Aspergillus flavus</i>	20 (40)
<i>Aspergillus fumigatus</i>	8 (16)
<i>Aspergillus niger</i>	4 (8)
<i>Aspergillus terreus</i>	2 (4)
No growth	16 (32)
Mucoromycosis	Nil

A. flavus: *Aspergillus flavus*, *A. fumigatus*: *Aspergillus fumigatus*, *A. niger*: *Aspergillus niger*, *A. terreus*: *Aspergillus terreus*, Histopathology showed all cases were *Aspergillus*

Table 7: CT scan of nose and sinus n=50

Sinus involvement	Number of patients (%)
Maxillary sinus	44 (88)
Ethmoidal sinus	38 (76)
Frontal sinus	24 (48)
Sphenoidal sinus	26 (52)
All sinuses	14 (28)
Orbital	10 (20)

Table 8: Unilateral/bilateral comparison study n=50

Sides of nose and sinuses	Number of patients (%)
Right	6 (12)
Left	8 (16)
Unilateral	14 (28)
Bilateral	36 (72)

Table 9: Complications n=50

BY A disease process	
Complication	Number of patient
1. Orbital complication Epiphora Proptosis	6 (12) 2 (4)
2. Intracranial	Nil

Table 10: Follow-up and recurrence

Number of cases	Month of follow-up	Number of recurrence
16 cases	18 months	4
24 cases	12 months	2
10 cases	6 months	-

Histopathological Examination

A total of 50 different fungal diseases have been reported in fungal sinusitis.

Aspergillus, ubiquitous fungus of the class ascomycetes is the most commonly encountered fungus in the environment and is the most common species encountered in fungal sinusitis generally and presumably in allergic fungal sinusitis. The latter is largely based on histopathological finding of fungi with morphologic features similar to *Aspergillus* and not on the basis of culture documentation. In our series,

100% of fungal sinusitis was histopathologically proven to be aspergillus.

In our study shows 100% allergic *A. sinusitis*. Klossek *et al.* in his case series of 100 cases documented that 94% were histopathologically proven allergic *A. sinusitis* various other organisms have reported as pathogens in allergic *A. sinusitis* caused by different fungi. *Bipolaris specifera* B, Australians, *Aspergillus*, *Alternaria* and *Curvularia lunata*. The identification of these fungi may be related to the improved ability of microbiology laboratories to identify the diverse hyphae with variation in the conical pores (Table 6).^{15,16}

In our study, all the cases of allergic *A. sinusitis* were sent for the fungal culture. In all the cases the material sent for culture were fungal mass taken from the infected sinus cavity. out of 50 cases 34 were culture positive for aspergillus and remaining 20 were *A. flavus*, 8 were *A. fumigates*, 4 were *A. niger*, and 2 were *A. terreus*. Rhinomucormycosis was no present in our study in histopathological examination.

In our studies, no other species of fungi was identified either on the HPE or cultural examination.

CT Scan of Nose and Sinuses

All our patients in this series underwent CT scan preoperatively, magnetic resonance imaging (MRI) scan was not considered due to the high cost factor and relatively low amount of extra information in cases of fungal diseases of nose and paranasal sinus.

In one of the studies has reported that in t2 weighted MRI images, there is a signal void corresponding to surgically proven areas of thick inspissated allergic mucin.

The authors agree with above study with respect to the CT findings. All patients in our series with allergic *A. sinusitis* demonstrated areas of high alteration centrally within involved sinus by CT. These areas corresponded to surgical findings of thick allergic mucin. Some cases demonstrate a starry sky pattern of material, which appeared to be calcium densities on bone windows. CT scanning has been very useful in defining the full extent to the disease. *A. sinusitis* often has a mixture of high and low-density areas within the sinuses. Bone windows allow a very accurate assessment of possible invasion (Table 7).

In general, only one series in involved with *Aspergillus* most commonly the maxillary sinus. In our study, maxillary sinus (88%) is the common involvement. Next ethmoid 80%, frontal sinus 52%, sphenoid sinus 44%, and all sinuses involvement 24%.¹⁷

Surgical Procedure

In our study, 50 cases were operated by endoscopic sinus surgery.

Endoscopic sinus surgery with less morbidity and mortality, clearance was total and recurrence rate is almost minimal in our steady. Even though in our cases, we had no complication acquired in functional endoscopic sinus surgery. Only in 6 cases recurrence was noted. None of the patients developed complication and patient were discharged next day itself. This correlates well with the previous study.

We treated our patient with steroids both topically and systemically. The use of tropical intranasal steroids id routine, and we restrict the use of systemic steroids. It is our experience that the tropical intranasal steroids alone when taken regularly are effective in preventing recurrence of the disease. However feels that tropical intranasal steroids and effectively only after a course of oral corticosteroids.

Antifungal agents were not used in any of our cases with allergic *A. sinusitis*. Similar reports have been published by many authors regarding the endoscopic approach is the sole approach in the treatment of allergic *A. sinusitis*. However, some author feels that external approach definitely has its plane in the treatment of this condition especially in cases of orbital (or) intracranial extension of this disease.

Complication

Complications of endoscopic sinus surgery have been as major and minor according to the degree of morbidity and treatment needed to prevent permanent serious sequelae.

Complications seen in our study includes intraoperative hemorrhage in 4 cases (8%) and no cerebrospinal leak (Table 9). Pneumocephalus and other reported major complication (Markmay *et al.*, 1994) includes orbital hematoma. Loss of vision, diplopia, epiphora, meningitis, brain abscess, and focal brain hemorrhage which were not seen in our study.

Intracranial complication can be prevented by not disturbing the mucosa lying against the roof of the ethmoid sinus. It is also worth remembering that the vertical bony wall of olfactory groove where the middle turbinate attaches to the roof of the ethmoid sinus may be extremely thin and should be avoided. The authors feel that two other guidelines may help to prevent cerebrospinal fluid leaks. (1) Instrumentations or suction cannulas should be placed into the nose or sinuses only under endoscopic guidance, (2) The basal lamella should be entered at a point farthest from the roof of the ethmoids posteriorly and inferiorly rather than anteriorly and superiorly.

Intraoperative hemorrhage severe enough to require blood transfusion is rare in our review none of them require blood transfusion. The authors agree with other reported studies that this kind of preoperative bleeding is mostly from the interruption of the sphenopalatine artery as it courses over the face of the sphenoid sinus, just above the arch of the posterior nasal choanae.

The most frequently encountered minor complication in our study 28% (14 cases) were synechia. This adhesion was usually seen between the middle turbinate and septum or lateral wall of nose careful handling of the tissue during surgery minimizes the chance of contact between the two adjacent raw surfaces. Careful post-operative cleaning of the sinus cavity will also help in the prevention of adhesion of the 50 patient in our study, 14 had synechia which were released in the outpatient department, and there was no recurrence.

Periorbital ecchymosis is the next minor complication and a total of 8%. These complications were seen after the endoscopic sinus surgery. This occurs usually due to violation of lamina papyracea. The authors agreed with other reported studies that the violation of the lamina papyracea occurs most commonly with uncinectomy during endoscopic sinus surgery.

Follow-up and Recurrence

Post-treatment endoscopic surveillance is essential for long-term success since recurrent disease is common. Furthermore, the patient symptoms alone are not a satisfactory measure for persistent/recurrent disease.

In this series, 16 of our patient were followed up for a period of 18-month after surgery. 24 patients were followed up for a period of 12-month and another 10 patients followed up for 6 months. We have not lost any patient during the follow-up treatment and proper medication. 4 recurrences were noted within 12 months (Table 10).

The author feels that the complete and radical removal of fungal debris and careful regular follow up with intranasal steroids and if required systemic steroids when employed judiciously will result in the best long-term result after surgery.¹⁸⁻²⁰

CONCLUSION

This study on fungal diseases of the nose and paranasal sinuses was conducted at ENT Department Government Theni Medical College Hospital on 50 cases all are allergic *A. sinusitis*.

The most common age group with fungal disease of the nose and paranasal sinuses was between 21 and 40 years of age. There was a clear female preponderance with 64% and male cases constituted 36%.

All patients in this study had nasal symptoms. The most common symptoms was headache seen in 76% of our cases. 50 patients (100%) presented with nasal mass either polyps or fungal mass. The ocular sign was seen in 16% of cases.

In our series of 50 cases, 50 (100%) histopathologically proven to be allergic *A. sinusitis*. Fungal culture showed that *A. flavus* (40%), *Aspergillus fumigatus* (24%), *A. niger* (8%), and *A. terreus* (4%) were culture positive and no mucormycosis present.

CT scan was found to be highly valuable in pre-operative evaluation and intraoperative guidance.

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