Clinical Study of Fungal Granulomatous Diseases

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ABSTRACT:

Introduction: Fungal Granulomatous disease is characterised by presence of granulomas with multinucleated giant cells and palisading histiocytes. Aspergillosis is the commonest fungal infection of the nose and sinuses. Mucomycosis is a polymorphic disease with diverse clinical manifestation. The disease has been described as having distinct clinical categories namely- rhinocerebral, pulmonary, cutaneous, gastrointestinal and disseminated.

Material and methods: In this study 10 cases of histologically diagnosed fungal granulomatous disease were studied on the basis of their age distribution, common symptoms, sex ratio, modality and response to treatment.

Results: In our study most of the patients were in the age group between 40-60 years. Mean age was found to be 45.4 years. Male were the predominant sex to be affected in the ratio of 4:1. Most common symptom were nasal obstruction, headache, epistaxis, nasal mass, nasal/facial deformities. Aspergillus species was found to be the predominant fungus for causation of the disease. Combined medical and surgical modality of treatment yielded good results in terms of recurrence and complications.

Conclusion: In the present study of fungal granulomatous conditions, presentation of the patients varied from nasal symptoms like nasal obstruction, nasal bleed, mass and nasal or facial deformity, in absence of more generalized symptoms. Clinical diagnosis is often difficult and has to be relied on KOH mounting and Histopathological examination of biopsy specimen. Mostly medical and surgical modalities have to be combined together according to clinical situation to reduce the morbidity and mortality.

Key Words: fungal granuloma, aspergillosis, mucormycosis, amphotericin B, FESS, Fluconazole

INTRODUCTION

The term Granuloma comes from the Latin ‘granulum’ which refers to a small particle or grain. Granulomatous inflammatory reaction has attracted a great deal of attention as it exhibits considerable variation both clinically and histologically. Granulomatous inflammation is a distinctive pattern of chronic inflammatory reaction characterized by focal accumulation of activated macrophages, which often develop an epitheloid appearance.

Granulomas of the nose and sinuses may be caused by specific or nonspecific agents. Most of these are a result of specific infections organism and are termed specific granulomas.
Fungal granulomatous disease are one of the more common and have an increased risk of complications. These granulomas are a common disease entity in tropical environment because of the prevailing high atmospheric temperature, humidity and contributory factors like poor hygiene, malnutrition.

**MATERIAL AND METHODS**

The present study was carried out on both the outpatients and inpatients of Department of ENT. Only those patients presenting with chronic symptoms of nasal obstruction, epistaxis, nasal discharge, deformity, showing nodules, ulceration and atrophic changes on clinical examination and histopathological diagnosis of fungal granulomatous disease were selected for this study. Ethical committee clearance was obtained prior to conducting study. The consent was taken from all the 10 cases. Mean age of the patient was found to be 45.4 years. A detailed history was taken and a thorough systemic and ENT examination with special emphasis on nodules, polyps, ulceration in the nasal cavity. Based on the clinical signs and investigation a diagnosis was arrived and appropriate medical or surgical or both modalities of treatment were carried out. The patients were followed up for a period of 6 months and special emphasis was given for the recurrence of the disease and recovery of the patient.

**RESULTS**

**Table no 1: Age distribution of the patients**

<table>
<thead>
<tr>
<th>Sl.no</th>
<th>Age Group</th>
<th>No of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0-10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>11-20</td>
<td>1</td>
<td>10%</td>
</tr>
<tr>
<td>3</td>
<td>21-30</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>31-40</td>
<td>2</td>
<td>20%</td>
</tr>
<tr>
<td>5</td>
<td>41-50</td>
<td>3</td>
<td>30%</td>
</tr>
<tr>
<td>6</td>
<td>51-60</td>
<td>3</td>
<td>30%</td>
</tr>
<tr>
<td>7</td>
<td>61 and above</td>
<td>1</td>
<td>10%</td>
</tr>
</tbody>
</table>

As depicted in the above table most of the patients were in the age group between 40-60 years. Mean age was found to be 45.4 years. In these 10 cases, youngest case being 14 year and oldest case being 70 years old. 4 patients in the study had diabetes mellitus.

**Table no 2: Sex distribution**

<table>
<thead>
<tr>
<th>Sl.no</th>
<th>Sex</th>
<th>No of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>8</td>
<td>80%</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>2</td>
<td>20%</td>
</tr>
</tbody>
</table>

As depicted in the above table male were the predominant sex to be affected in the ratio of 4:1

**Table no 3: Mode of presentation**

<table>
<thead>
<tr>
<th>Sl.no</th>
<th>Mode of presentation</th>
<th>No of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nasal obstruction</td>
<td>8</td>
<td>80%</td>
</tr>
<tr>
<td>2</td>
<td>Epistaxis</td>
<td>4</td>
<td>40%</td>
</tr>
<tr>
<td>3</td>
<td>Headache</td>
<td>5</td>
<td>50%</td>
</tr>
<tr>
<td>4</td>
<td>Nasal mass</td>
<td>3</td>
<td>30%</td>
</tr>
<tr>
<td>5</td>
<td>Nasal/ facial deformity</td>
<td>2</td>
<td>20%</td>
</tr>
</tbody>
</table>

Most common symptom were nasal obstruction, headache, epistaxis, nasal mass, nasal/facial deformities.

**Table 4: Distribution of fungal species**

<table>
<thead>
<tr>
<th>Sl.no</th>
<th>Species</th>
<th>No of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Aspergillus</td>
<td>8</td>
<td>80%</td>
</tr>
<tr>
<td>2</td>
<td>Mucor</td>
<td>2</td>
<td>20%</td>
</tr>
</tbody>
</table>

Aspergillus species was found to be the predominant fungus for causation of the disease. Nine patients underwent fungal debridement by FESS, one patient of aspergillosis underwentfungal debridement with orbital decompression for orbital cellulitis and one patient of rhinocerebral mucormycosis expired during the course of treatment prior to surgical intervention. 8 patients recovered completely during the course of study and follow up period of 6 months. 1 patient of rhinocerebral mucormycosis expired during the course of
treatment and 1 patient of mucormycosis developed recurrence.

**DISCUSSION:**
Fungal Granulomatous disease is characterised by presence of granulomas with multinucleated giant cells and palisading histiocytes. Factors predisposing to invasive fungal granulomatous diseases include immunocompromise, poorly contributed diabetes mellitus, haematological malignancies, severe burns, renal disease, AIDS, iatrogenic immune suppression after renal transplantation, deferoxamine therapy. Acidosis and hyperglycaemia are an ideal environment for fungal growth, especially because such metabolic condition inhibit the affinity and effectiveness of macrophages altering host defense mechanism. Aspergillosis is the commonest fungal infection of the nose and sinuses and seven pathogenic species have been identified. Of these A. fumigatus accounts for 90% followed by A. niger and A. flavus. Aspergillus infection of the nose and sinus can occur anywhere and at any age. Two forms are usually described granulomatous and non granulomatous based on the presence or absence of granulomas within tissue. It occurs in healthy individuals sometimes after a previous history of chronic rhinosinusitis. It may also been seen in immuno compromised individuals.

It is characterised by a clinical presentation where pain is the main symptom. An asymptomatic period frequently occurs, symptoms appearing only when the orbit or skull base are involved. Chronic headache, proptosis and cranial nerve deficits have been reported. The maxillary sinus seems to be the major site.

Mucormycosis is a polymorphic disease with diverse clinical manifestation. The disease has been described as having distinct clinical categories namely- rhinocerebral, pulmonary, cutaneous, gastrointestinal and disseminated. Rhinocerebral mucormycosis is the commonest form accounting for between a third and a half of all cases.

Incidence of rhinocerebral mucormycosis is not influenced by age or gender. Most commonly isolated organism in patients with mucor are of this family: Rhizopus, rhizomucor (mucor) and alcidia. The spectrum of disease presentation in rhinocerebral mucormycosis is wide, ranging from localised paranasal sinus disease to extensive orbital and intracranial involvement with associated neurologic deficit. It may initially present with symptoms consistent with either sinusitis or periorbital cellulitis. Cranial spread may initially be relatively asymptomatic. With extensive intracranial involvement, the mortality increases considerably due to encasement and thrombosis of major intracranial vasculature. Intracranial extension has been shown to be the cause of death in 80% of cases and the infection is considered to be almost invariably fatal in the presence of intracranial extension. Poorer prognosis include orbital involvement, immunosuppressive therapy, diabetic ketoacidosis, delayed diagnosis and medical management without surgical debridement.

**Diagnosis:**
Diagnosis is based on following battery of investigations.

i) Direct microscopy on KOH preparation

ii) Histopathology – reveals a typical granuloma with multinucleated giant cells and palisading histiocytes with fungal invasion of bone, mucus membrane and bone. In Mucormycosis angioinvasion can be present.

iii) Culture is rarely sufficient for diagnostic purposes after fungi are ubiquitous and difficult to isolate but can be helpful in identifying the causative fungal species.

iv) CT scan – evidence of bony erosion and mucosal thickening in appropriate clinical context is strongly suggestive.

v) MRI – Enables early detection of meningeal, intraparenchymal and intracranial vascular occlusion.

**Treatment:**
Granulomatous Invasive Aspergillosis:
- Surgical debridement to remove the granulomas
- Antifungal agents like Fluconazole 150 mg once daily for 7-14 days.

A long term follow up and radiological followup is required to identify and treat recurrent disease.  

Mucormycosis:
- Medical – Amphotericin B deoxycholate
- Liposomal amphotericin B
- Oral Itraconazole 100 mg daily
- Hyperbaric oxygen helps alleviate acidosis and are thought to improve neutrophils ability to phagocytose.

Surgical – Debridement of infected and necrotic tissue is considered an essential component of an optimal treatment regimen. Role of endoscopic sinus surgery has been demonstrated as a conservative approach.  
- Orbital extraction in cases of orbital invasion.

In a study conducted by Andrews G et al. of sinonasal fungal granulomas of 50 patients, 29 patients (58%) were of aspergillosis followed by mucormycosis in 14 patients (28%). Our study correlates with this study, having 8 cases (80%) of Aspergillosis as predominant type. One patient of aspergillosis underwent debridement under endoscopic sinus surgery with orbital decompression along with IV Amphotericin-B. One patient underwent debridement under endoscopic sinus surgery along with IV Amphotericin-B. This treatment was in accordance with the study of Andrews G et al and Klossek JM et al. Six cases of Non invasive type were seen in immunocompetent patients and underwent debridement under endoscopic sinus surgery along with oral fluconazole 150 mg OD for 2 weeks. No relapse was seen.

2 cases of mucormycosis were seen, both the patients were immunocompromised (uncontrolled diabetes) and had palatal perforations.  

1st case was of rhinocerebral variety with orbital involvement and diabetes mellitus with ketoacidosis and the patient expired during the course of treatment. In a similar study by Peterson KL et al in which 3 patients (37.5%) of 32 patients of Rhinocerebral mucormycosis with diabetes mellitus with ketoacidosis expired during the course of treatment. The study showed that patients of rhinocerebral mucormycosis with orbital involvement, treated only medically had a mortality of 75%.

2nd case was rhino-sinusal mucormycosis who has undergone multiple debridements along with antifungal treatment (T. Fluconazole) due to non affordability for IV Amphotericin, and was still undergoing treatment and follow up. Palatal perforation in this patient was closed by dental plate prosthesis.

CONCLUSION:

In the present study of fungal granulomatous conditions, presentation of the patients varied from nasal symptoms like nasal obstruction, nasal bleed, mass and nasal or facial deformity, in absence of more generalized symptoms. Clinical diagnosis is often difficult and has to be relied on microbiological KOH mounting and Histopathological examination of biopsy specimen. Many a times they may be overlooked in clinical practice as simple case of bacterial diseases. Lack of definite protocols for treatment, difficulties in diagnosing the disease clinically, correction of the deformities and treating the complications arising makes it more challenging. Mostly medical and surgical modalities have to be combined together according to clinical situation to reduce the morbidities. And medical line should be continued for a long time to prevent recurrence and prevent complications arising from the disease.

Awareness regarding the disease process and health education should be provided to people regarding maintenance of hygienic conditions and utilization of health care facilities

REFERENCES:

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