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Research Paper

Role of Allergic mucin in Allergic Fungal Rhinosinusitis

Medical Science

KEYWORDS : AFRS; allergic mucin; peanut butter mucin; fungal rhinosinusitis

Dr. Tanvi Anoop Lohiya — Senior Registrar Department of ENT & Head-Neck Surgery Lokmanya Tilak Municipal Medical College & General Hospital

Kshitij Dhaval Shah — Assistant Professor, Department of ENT & Head-Neck Surgery Lokmanya Tilak Municipal Medical College & General Hospital

Dr. Renuka Anil Bradoo — Professor & Head Department of ENT & Head-Neck Surgery Lokmanya Tilak Municipal Medical College & General Hospital

ABSTRACT

AFRS is a non-invasive form of fungal rhinosinusitis which develops as a Type I hypersensitivity to fungus. Patients commonly present with chronic rhinosinusitis with nasal polyps, inhalant atopy, elevated total serum immunoglobulin E (IgE), and sinus-obstructing inspissates of a characteristic extramucosal 'peanut buttery' eosinophil-rich material called 'allergic mucin' that contains sparse numbers of fungal hyphae and CT findings of "double densities" The treatment is surgery, complemented by medical therapy in the form of systemic steroids or antifungals such as Itraconazole. This study has been undertaken to assess the significance of allergic mucin in AFRS. The study concludes that allergic mucin has a strong positive correlation and hence is a major diagnostic criteria for AFRS.

Introduction:

Allergic fungal rhinosinusitis (AFRS) is the most common type of fungal rhinosinusitis [1]. It is a non-invasive form of allergic hypertrophic rhinosinusitis, representing a hypersensitivity response to the presence of extramucosal fungi within the sinus cavity. AFRS has distinct clinical, histopathological, and prognostic findings that differentiate it from other forms of sinusitis. Clinically and immunologically it appears analogous to allergic bronchopulmonary aspergillosis (ABPA) [2]. The overall incidence of AFRS is estimated at 5% to 10% of all cases of chronic rhinosinusitis requiring surgery [3].

AFRS is a truly unique pathologic entity, defined largely by the presence of allergic fungal mucin in the sinuses. It has characteristic radiological findings in the form of hyperattenuating areas (double densities) within opacified sinuses on CT scan (4). Fungal-specific IgE (positive allergy skin test), IgG to the etiologic fungus, presence of atopy to common aeroallergens, and immunocompetence are clinical findings that are always present and support the diagnosis of AFRS. The treatment is a multipronged approach including surgery and medical therapy in the form of systemic steroids or antifungals such as Itraconazole (5). This form of fungal rhinosinusitis has the best prognosis.

This is a single-centre prospective study, undertaken to determine the incidence of allergic mucin in patients with AFRS, and its role in the outcome after treatment with systemic anti-fungals and steroids.

Materials & Methods:

30 patients of chronic rhinosinusitis fulfilling at least three of Bent and Kuhn's major criteria (6) for the diagnosis of allergic fungal sinusitis, were included in the study, from 2011 to 2013.

A diagnostic nasal endoscopy under local aneasthesia was carried out for each patient. Fungal debris, if found, was sent for KOH mount for fungal hyphae and fungal culture. A CT scan of the paranasal sinuses, with axial and coronal cuts, bony and soft tissue windows was done. Sagittal reconstruction was asked for in cases with disease in frontal recess, erosion of posterior wall of frontal sinus or erosion of cribriform plate. Surgical anatomy, sinuses involved, bony erosions of lamina papyracea and skull base were noted. Routine investigations for fitness for general anaesthesia, with differential leukocyte count and absolute eosinophil count were carried out.

Each patient underwent endoscopic sinus surgery with clearing of polyps, allergic mucin and fungal debris from all the paranasal sinuses. Special attention was given to washing out of all the allergic mucin and fungal debris, restoration of sinus ventilation and preservation of mucosa. The obtained allergic mucin and fungal debris were sent for KOH mount for fungal hyphae and fungal culture. Debrided tissue was sent for histopathological assessment. Nasal packs were kept for two days.

Post operatively, patients were given tablet Itraconazole (systemic antifungal) 100 mg BD, and Prednisolone (systemic steroid) 1 mg/kg in tapering doses, once in the morning on full stomach along with antacids. After removal of nasal packs, patients were put on steroid sprays and discharged from the hospital. Alkaline nasal douches were given for clearance of nasal crusts.

Each patient was reviewed with Nasal endoscopy – immediate 1 week post-surgery, then after 15 days, 1, 2, 3 and 6 months. Decision to continue inhalational steroids and Itraconazole was taken on the basis of the postoperative endoscopic findings.

The outcome of the treatment was assessed on the basis of endoscopic findings at the end of 6 months as per Kupferberg staging system (7). As per this system, in each stage, A represents absence of allergic mucin and B represents presence of allergic mucin.

Stage 0 (A/B) – No mucosal oedema – excellent outcome
Stage I (A/B) - Mucosal oedema – good
Stage II (A/B) - Polypoid oedema – satisfactory
Stage III (A/B) - Sinus polyps - recurrence

Patients with non-resolution of complaints or recurrence of symptoms also underwent endoscopic examination. CT scan was repeated in those cases with recurrence of polyps and those who had intra orbital and intra cranial extension on presentation.

Observations & results:

The study includes thirty patients, out of which twenty were males and ten females; the oldest patient was seventy years old and the youngest ten. Nineteen had bilateral pathology, eight left sided and three right sided.

Four patients had come with recurrent disease, operated elsewhere. One of the patients had been operated with a septoplasty for the nasal complaints.

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Seventeen patients had used inhalational steroids pre operatively. Seventeen patients had septate hyphae on KOH mount. Itraconazole was given to eleven of those patients. Twenty patients were given postoperative systemic steroids. Post operatively, inhalational steroids were given to all the patients.

Twenty patients had Kupferberg grade I A at 6 months. Four had grade II A. one patient had III A. One had I A on same side; IV B on unoperated side - posted for surgery in near future.

Five patients operated at the institute developed recurrence. One of them, on the same sites as before underwent surgery and was disease free at the end of six months. One patient developed recurrence three months post-surgery, was treated with systemic steroids and stayed disease free. Two patients had minimal recurrence and recovered with inhalational steroids. The fifth one remained disease free on the operated side, but developed it on the other side.

ASSOCIATION BETWEEN ALLERGIC MUCIN AND OUTCOME

Allergic Mucin	Outcome			
	Excellent	Good	Satisfactory	Recurrence
Yes (N = 27)	-	22	04	01
No (N = 03)	-	03	-	-

By Fisher Exact Test P > 0.05

There is a significant correlation between the presence of allergic mucin and AFRS. Allergic mucin was found in 90 percentage of patients with AFRS. Therefore we can conclude that allergic mucin has a strong positive correlation and hence is a major diagnostic criteria for AFRS. These patients responded well to endoscopic clearance and oral Itraconazole. 81 percent of patients with allergic mucin had good outcome i.e minimal mucosal edema at the end of six months. Complete clearance of allergic mucin from the paranasal sinuses leads to better post operative results.

Discussion:

AFRS is a truly unique pathologic entity, defined largely by the presence of allergic fungal mucin, which is a thick, tenacious, eosinophilic secretion with characteristic histologic findings.

The age group affected is predominantly young adults and adolescents, younger than most CRS patients, with a mean age at diagnosis of 21.9 years [3,8]. Most studies demonstrate a fairly equal male-to-female ratio (3). Since the causative organism, fungi, thrive well in warm and humid conditions, it is commonly seen in tropical countries such as India (3). The common causes of allergic fungal sinusitis are the dematiaceous hyphomycetes including Curvularia sp.,Bipolaris sp.,Pseudallescheria boydii, and the hyaline hyphomycetes such as Aspergillus sp. and Fusarium sp (9).

It is important to note that examination of the unique allergic fungal mucin itself, and not the surrounding mucosa, is the most reliable indicator of disease. Grossly, this thick, highly viscous, variably colored mucin has been described as being similar to peanut butter or axle grease and contains laminated accumulation of intact and degenerating eosinophils, Charcot-leyden crystals, cellular debris and sparse hyphae.

Microscopically, the mucin often takes on a chondroid appearance with sheets of eosinophils, frequently with the presence of eosinophilic breakdown products or Charcot-Leyden crystals that can easily be seen with H&E staining. Fungi themselves do not stain with H&E staining; however, their negative image can sometimes be appreciated. Special stains containing silver are usually needed to appreciate the branching, noninvasive fungal hyphae. Gomori Methenamine Silver staining shows small areas of sparsely scattered fungal hyphae within the allergic mucin (10).

Allergic mucin that is grossly and histopathologically identical to that found in AFRS has also been reported occasionally in hypertrophic sinus disease patients in the absence of AFRS. The allergic mucin is negative for fungal hyphae on histopathology, and surgical sinus fungal cultures are uniformly negative. The clinical presentation of such hypertrophic sinus disease patients is often similar to that of patients with AFRS, including the finding of intrasinus hyperattenuation on CT. Some of these patients, however, are nonatopic; many also have ASA/NSAID hypersensitivity. It has been suggested that this form of hypertrophic sinus disease be termed eosinophilic mucin rhinosinusitis (EMRS) [11].

Patients with residual allergic mucin have a greater chance of developing recurrence of the disease. Hence it is important to thoroughly wash out the allergic mucin in such patients to minimize the rates of recurrence.

AFRS is a medical disease requiring surgical intervention to ensure optimal results. It is a relatively new clinical entity with characteristic features. A high index of suspicion in young immunocompetent patients presenting with chronic rhinosinusitis is required for early diagnosis. Presence of allergic mucin is diagnostic for AFRS. Differentiation from invasive forms of fungal sinus disease is crucial, as the management as well as prognosis vary in the two. Endoscopic evaluation and radiological assessment are the cornerstones of diagnosis. A multimodality approach is required (medical, surgical and immunomodulation) as the disease is multifactorial. The exact role of anti fungals and systemic steroids in achieving systemic control of the disease can probably be established by larger population studies. Long term follow up is essential so that medical therapy, if required can be continued and recurrence prevented.

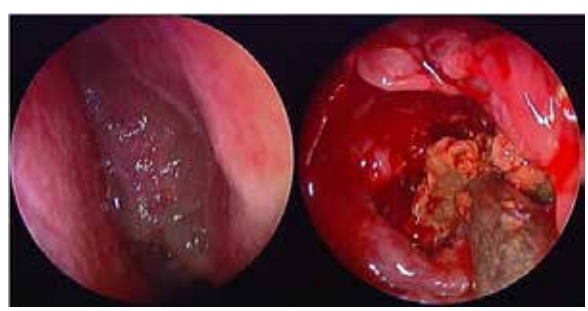

Figure 1: Endoscopic image of polyps and allergic mucin

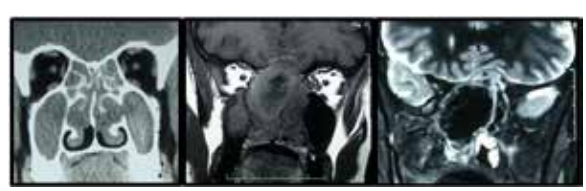

Figure 2: Radiological features:

CT coronal soft tissue – double densities
Iso to hypo intense on T1 weighted MRI
Signal void in T2 weighted MRI

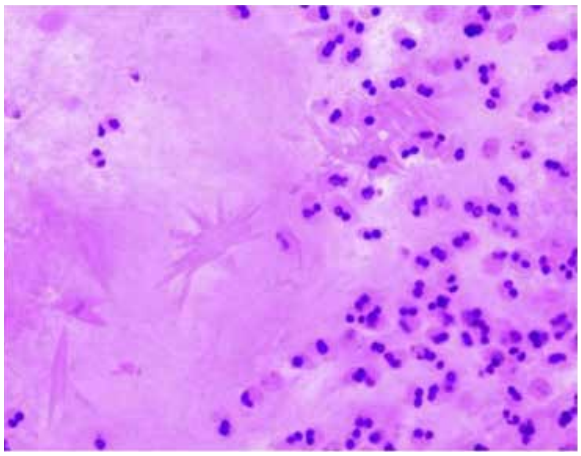

Figure 3: Charcot-Leyden crystalson a hematoxylin & eosin stain of allergic mucin

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