Evaluation of Diagnostic Criteria for AFRS: A Hospital Based Study

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ABSTRACT

Introduction

Bent and Kuhn criteria are the most commonly accepted diagnostic criteria for diagnosis of Allergic Fungal Rhinosinusitis. Other diagnostic criteria for the diagnosis of Allergic Fungal Rhinosinusitis include unilateral nasal disease, Charcot Leyden crystals, bony erosions which form the minor criteria in the diagnosis of Allergic Fungal Rhinosinusitis. Clinical and Laboratory features in Allergic fungal rhinosinusitis are variable. These variations in the diagnostic criteria in the diagnosis of Allergic Fungal Rhinosinusitis have been analysed in the present study.

Materials and Methods

Prospective study was performed on group of 46 patients of Allergic fungal Rhinosinusitis presenting in the Otorhinolaryngology OPD with symptoms of Allergic fungal rhinosinusitis as diagnosed and persisting for more than 3 months during September 2009 to August 2010.

Results

Absolute eosinophil count was elevated in 80.43%, total serum IgE elevated in 69.67%, skin prick test was positive in 63.05% of patients. CT scan revealed that most common paranasal sinus involved is ethmoid sinus as seen in 73.91% cases., Sphenoid sinus was least involved as seen in 17.40% cases. More than one paranasal sinus were involved in 65.21% of the cases.,Complete opacification of all sinuses with calcified deposits were seen in 4.76% cases. Mucosal thickening was seen bilaterally in 73.91% of the patients and bony erosion was noted in 6.52% of patients. Histopathology of nasal smears revealed Eosinophilia in 80.43% of patients. Inflammatory Charcot Leyden crystals were found in 15.21% of the patients45.65% showed goblet cell hyperplasia . Other types of inflammatory cells were seen in 56.52%of the study population and 23.91% patients showed positive fungal hyphae.

Discussion

The significance of absolute eosinophil count, skin prick test, histopathology, CT Scan features and nasal smear cytology have been discussed along with review of literature.

Conclusion

Although management of Allergic Fungal Rhinosinusitis has advanced tremendously with better understanding of underlying pathogenesis, diagnostic strategies are still far from clear and are still emerging. Lot of research work has to be carried out regarding relevant diagnostic criteria for the disease.

Keywords:

Rhinitis, Allergic; Sinusitis; Eosinophils; Immunoglobulin E; Skin Tests, Mucins

Allergic fungal rhinosinusitis is observed to be a non-invasive disease involving the nose and paranasal sinuses and it is believed to be due to hyper-reactivity to fungal antigens. Patients of allergic fungal rhinosinusitis suffer from allergic rhinitis, and most of these patients have increased blood levels of immunoglobulin E (IgE).[1] The exact pathophysiology of the disease spectrum is not clearly understood. However it is believed that fungal allergens elicit immunoglobulin E mediated allergic and possibly type III immune complex mediated mucosal inflammation in the absence of invasion in an immunocompetent individual.[2]

Most commonly accepted diagnostic criteria for diagnosis of Allergic Fungal Rhinosinusitis are Type I hypersensitivity, nasal polyposis, eosinophilic mucin,

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CT findings, and fungal staining which form the basis of Bent and Kuhn criteria. Other diagnostic criteria for the diagnosis of Allergic Fungal Rhinosinusitis include unilateral nasal disease, Charcot Leyden crystals, bony erosions which form the minor criteria in the diagnosis of Allergic Fungal Rhinosinusitis.[3]

Investigations for diagnosis of Allergic Fungal Rhinosinusitis in India are grouped as in-vivo and in-vitro diagnostic techniques. In-vivo methods of investigation of the disease process include skin-prick test, intradermal test, bronchial challenge test and nasal challenge test. In-vitro investigations include radioallergosorbent test (RAST), enzyme linked immunosorbent assay (ELISA), microarray and immunocap are applied to arrive at diagnosis.[4]

Radioallergosorbent test (RAST) is an in-vitro test for diagnosing IgE in serum for environmental allergens. ELISA gives the amount of IgE circulating in the blood during sensitization by an allergen.[5] It was observed by the research work performed in this area that the in-vitro tests are more sensitive than in-vivo tests. Though RAST or ELISA is preferred to be more precise investigations in diagnosis of allergic diseases, they are expensive and hence are not commonly preferred in the diagnosis of Allergic Fungal Rhinosinusitis. Also the role of these tests are believed to be limited in India for diagnosis of allergic diseases as purified proteins and antibodies for these tests are not available for characterization based on major allergen content in India.[6]

The investigative criteria for diagnosis of Allergic Fungal Rhinosinusitis have undergone numerous revisions.[7] Apart from haematological investigations used for detecting underlying pathology in allergic fungal rhinosinusitis, most authors agree on non-contrast CT scan in rhinosinusitis demonstrating hyperattenuating allergic mucin within the lumen of the paranasal sinus and the presence of non-invasive fungal elements within that mucin, detectable on staining or culture as diagnostic criteria in allergic fungal rhinosinusitis.[8]

Although the management of allergic fungal rhinosinusitis has advanced tremendously with better understanding of the underlying pathogenesis, the diagnostic strategies are still far from clear and are still emerging. The purpose of this study is to identify the sufficiency of the present investigations in the diagnosis of Allergic Fungal Rhinosinusitis by observing the values of absolute eosinophil count, total serum IgE and skin prick test in patients of allergic fungal rhinosinusitis while correlating the clinical diagnosis of allergic fungal rhinosinusitis with histological confirmation by nasal smear cytology.

Materials and Methods

A prospective study was performed on a study group of 46 patients of Allergic Rhinosinusitis presenting in OPD, Department of Otorhinolaryngology with symptoms of the disease persisting for more than 3 months during September 2009 to August 2010 to observe the values of absolute eosinophil count, total serum IgE and skin prick test in patients of allergic fungal rhinosinusitis and also to study the variation in clinical diagnosis of Allergic Fungal Rhinosinusitis with histological diagnosis and nasal smear cytology.

Patients in the age group of 20 to 60 years with no sex predilection with a clinical history of Allergic Rhinosinusitis with symptoms of nose block, headache, nasal itching, sneezing, rhinorrhoea for more than 3 months who were not responsive to medications were included in the study group.

Patients having symptoms of Allergic Rhinosinusitis for less than 3 months were excluded from the study, as also the patients having bronchial asthma, atopic dermatitis and immunosuppressive diseases. Allergic Fungal Rhinosinusitis is mainly believed to be due to Type I hypersensitivity and Type III reaction and formation of immune complexes in the disease spectrum is doubtful thus excluding the involvement of systemic diseases from the study. These minor criteria of Bent and Kuhn in diagnosis of Allergic fungal Rhinosinusitis always need not be present in all the patients with allergic fungal rhinosinusitis.

After obtaining a written informed consent, the patients were evaluated with a clinical questionnaire for clinical symptoms of headache, nasal obstruction, nasal itching, sneezes and rhinorrhoea. Diagnostic nasal endoscopy was performed in all the patients to observe for anatomical abnormalities, shiny allergic mucin and

any space occupying sino-nasal polyposis in the nasal cavity.

The patients were investigated with absolute eosinophil count, total serum IgE, and skin prick test. CT scan of paranasal sinuses Coronal cuts 2 mm thickness with axial reconstruction was performed in all these patients. Nasal lavages were collected from the patients to study nasal smear cytology and histopathological examination.

These specimens were examined using light microscopy after digestion with 10% potassium hydroxide (KOH). Haematoxylin and Eosin stains were used for all sections in histopathological examination. Other special stains were used as and where required. Histopathological findings of allergic mucin consisting of degenerating eosinophils, cellular debris, Charcot Leyden crystals inflammation, and presence of fungal hyphae were recorded. Samples were cultured onto Sabouraud's dextrose agar and incubated for 4 weeks as and where required.

Results

In the present study laboratory investigations of absolute eosinophil count revealed elevated levels in 80.43% of patients. Total serum IgE was elevated in 69.67% of patients. Skin prick test performed with CREDISOL® reagents on the forearm of the patients for allergens based on local climatic conditions with positive control of histamine and negative control of normal saline was positive in 63.05% of patients.

CT scan findings in the present study revealed that the most common paranasal sinus involved being the ethmoid sinus in 73.91% of patients while sphenoid sinus was the least commonly involved sinus in 17.40% of patients. Involvement of more than one paranasal sinus was the common finding in this study and it was observed in 65.21% of patients.

Complete opacification of sinuses with calcified deposits was observed in 4.76% patients in the present study. Mucosal thickening was observed bilaterally in 73.91% of patients. Bony erosion was observed in 6.52% of patients. These results were tabulated in table I.

Histopathology of the specimens of nasal smears revealed that Eosinophilia was the most common finding in 80.43% of patients. Predominance of eosinophils is usually observed in patients of Allergic fungal rhinosinusitis.[9] For quantification of Eosinophils cells in the nasal smears we propose Grading of AFRS based on number of Eosinophils observed per high power field.

Table I: CT scan findings in Allergic Fungal Rhinosinusitis (N=46)

	CT SCAN FINDINGS	NO OF CASES N=46	%
Sinus involved	Ethmoid	34	73.91
	Frontal	24	52.17
	Maxillary	32	69.57
	Sphenoid	8	17.4
	Multiple sinus involvement	30	65.21
Sinus opacification	Partial	18	39.13
	Complete	28	60.87
	Complete with calcification	2	4.76
Mucosal thickening	Unilateral	12	26.08
	Bilateral	34	73.91
Bony erosion	Present	3	6.52

Table II: Grading of Eosinophilia

NO. OF EOSINOPHILS	GRADING OF EOSINOPHILIA
1-10 per HPF	1+
10-25 per HPF	2+
25-50 per HPF	3+
>50 per HPF	4+

In the present study the patients having elevated levels of Eosinophils were observed in the 3+, 4+ grading of eosinophils and hence were classified as Eosinophil rich. The method of quantification of grading of Eosinophils is mentioned below in Table II.

Inflammatory Charcot Leyden crystals were observed in 15.21% of patients, Goblet cell hyperplasia was observed in 45.65% of patients. Other types of inflammatory cells were observed in 56.52% of patients. It was observed that only 11 (23.91%) patients of the present study showed positive fungal hyphae microscopically. These results were tabulated in Table III.

In the present study when the investigations of total serum IgE, AEC, Skin prick test was compared with nasal smear cytology there was a variation in diagnosis in 4.34% of the patients. These results were documented in Table IV.

Table III: Histopathology of nasal smear in Allergic Fungal Rhinosinusitis (N=46)

HISTOPATHOLOGY	NO OF CASES N=46	%
Allergic mucin	36	78.26
Charcot laden crystals	7	15.21
Fungal hyphae	11	23.91
Goblet cell Hyperplasia	21	45.65
Eosinophilia	37	80.43
Other cells increase	26	56.52

Table IV: Diagnosis of Allergic Fungal Sinusitis (N=46)

	NO OF PATIENTS N=46	%
Clinical diagnosis of Allergic Fungal Sinusitis	24	52.17
Histopathological diagnosis of Allergic Fungal Sinusitis	22	47.83
Change in diagnosis	2	4.34

Discussion

In this study, clinically 46 cases were diagnosed to have Allergic Fungal Rhinosinusitis based on the clinical findings. The mean age of our cases was 29.4 years with a range of 20–60 years. A slightly higher incidence of the disease was observed in the females with the male: female ratio of 1: 1.19. The findings of our study were similar to the study by Kaur et al.[10]

In the patients diagnosed as suffering with allergic fungal rhinosinusitis clinically, laboratory investigations of absolute eosinophil count revealed elevated in 80.43% of patients. Total serum IgE was elevated in 69.67% of patients. Eosinophilic count higher than 500 cells per ml was considered as serum eosinophilia while IgE levels were considered to be raised when the counts were >100U/ml.[11] Eosinophilia is observed to be one of the minor criteria useful for diagnosis of Allergic fungal

rhinosinusitis.[12]

Skin prick test was positive in 63.05% of patients. Skin test reactivity depends on at least three separate factors: (1) an intact immune system; (2) the presence of IgE sensitized mast cells that release mediators when exposed to antigen; (3) and skin that can respond to histamine with the development of inflammatory response including erythema and induration.[13] However a negative skin prick test in patients of allergic fungal rhinosinusitis is presumed as a probability of vasomotor aetiology

The presence of allergic mucin in histopathology specimens forms an important diagnostic criterion in addition to the demonstration of fungal elements in diagnosis of Allergic fungal rhinosinusitis.[14] In the present study Allergic mucin was observed in 78.26% of patients and cheesy debris was observed in 48.70% in the nostrils of the patients. The lower percentage of allergic mucin in patients of allergic fungal rhinosinusitis can be attributed to the usage of indiscriminate use of corticosteroids which might have probably disturbed the mucin blanket.

CT scan findings form one of the important diagnostic criteria in the diagnosis of allergic fungal rhinosinusitis. The usual radiological findings of the disease process include pan sinus disease with expansion and smooth thinning of the affected sinuses with thin peripheral enhancement with no enhancement noted in the central sinus contents. There is usually involvement of multiple sinuses.[15] In the present day scenario there is a need for a specific radiological classification for Allergic Fungal Rhinosinusitis where there is a scope of lot of research in this area.

Nasal smears cytology revealed that Eosinophilia was the most common finding in 80.43% of patients. Inflammatory Charcot Leyden crystals were observed in 15.21% of patients, Goblet cell hyperplasia was observed in 45.65% of patients. Other types of inflammatory cells were observed in 56.52% of patients. These other types of cells observed were attributed to neutrophil predominance which may be due to an acute bacterial Rhinitis. It was observed that 11 (23.91%) patients of the present study showed positive fungal hyphae microscopically.

It can be considered to evaluate Allergic Fungal Rhinosinusitis based on Antigen specific IgE, microscopic evaluation of allergic mucin obtained for evaluation of degranulation products and proteins obtained after degranulation and serological testing of precipitating antibodies.[16] However in developing countries like India owing to the cost effectiveness of the above investigations these are not routinely available for the diagnosis of the disease spectrum of Allergic Fungal Rhinosisnusitis.

Conclusion

In the present day clinical scenario despite the newly emerging clinical investigations and efforts, allergic fungal rhinosinusitis remained an entity which is difficult to diagnose. With the description of newer categories like eosinophilic fungal rhinosinusitis and eosinophilic mucin rhinosinusitis, it has become more difficult to establish criteria for diagnosis.

At the present time it is likely that initiation of the inflammatory cascade leading to allergic fungal rhinosinusitis is a multifactorial event, requiring the simultaneous occurrence of such things as IgE-mediated sensitivity, specific T-cell HLA receptor expression, exposure to specific fungi, and aberration of local mucosal defence mechanisms.[17]

There exists a controversy regarding the documented reports of histologic invasion in possible cases of allergic fungal rhinosinusitis. Thus it can be considered that apart from clinical diagnosis, type I hypersensitivity, Eosinophilia, Charcot-Leyden crystal may also be considered important criteria to define this entity.

Although the management of allergic fungal rhinosinusitis has advanced tremendously with better understanding of the underlying pathogenesis, the diagnostic strategies are still far from clear and still emerging. As clinical evidence of allergic fungal rhinosinusitis emerged, controversy regarding its diagnosis remained naive still and despite past and current efforts, many of these controversies remain incompletely resolved. Continuing clinical study has illuminated some aspects of the disease but still lot of research work has to be carried out regarding the relevant diagnostic criteria for the disease. The possibility of

inclusion and usefulness, efficacy of Antigen specific IgE, microscopic evaluation of allergic mucin obtained for evaluation of degranulation products and proteins obtained after degranulation and serological testing of precipitating antibodies in the diagnostic criteria for Allergic Fungal Rhinosinusitis can be considered.

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