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Sensitization to *Aspergillus* Antigens in Perennial Rhinitis

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SUMMARY **This study was conducted to determine the frequency of sensitization to *Aspergillus* antigens in 27 patients with perennial rhinitis. Immediate cutaneous reactivity was observed in 7 (26%) patients. In 3 of these 7 patients, hypersensitivity was restricted to *Aspergillus* antigens alone. One patient had an isolated late cutaneous reaction. Hypersenstivity was observed most commonly with *A.flavus*. Serum precipitins to *A.flavus* were detected in one patient. It is possible that sensitization to *Aspergillus* antigens may play an important role in the causation of perennial rhinitis and could also increase the risk of developing other *Aspergillus* associated hypersensitivity respiratory disorders subsequently.**

Aspergillus, a highly ubiquitous mold, is known to cause four distinct clinically recognizable forms of hypersensitivity respiratory disorders viz. allergic bronchopulmonary aspergillosis (ABPA), IgE mediated asthma, hypersensitivity pneumonitis and allergic *Aspergillus* sinusitis (AAS).[1] Prevalence of sensitization to *Aspergillus* antigens has been documented in asthmatics[2]but there exists an uncertainty regarding similar data in patients with perennial rhinitis. Such information assumes importance as *Aspergillus* is now known to cause AAS, a hypersensitivity disorder which may involve the upper respiratory tract either alone[3] or along with the lower respiratory tract.[4] A preliminary study was therefore conducted to determine the frequency of sensitization to *Aspergillus* antigens in patients with perennial rhinitis in India.

MATERIALS AND METHODS

The study population comprised 27 consecutive patients with perennial rhinitis of more than one year duration who were attending the Clinical Research Center of the Vallabhbhai Patel Chest Institute Patients with history suggestive of concomitant bronchial asthma or sinusitis were excluded as were those patients who had received immunotherapy. Clinical assessment of all patients was done along with haemogram, routine pulmonary function tests and roentgenograms of the chest and paranasal sinuses (Water's view). Skin tests were performed on the forearm by the intracutaneous technique with antigens of *Aspergillus fumigatus, A.flavus, A.niger* and *A.tamarii* in dilution of 1:50 (0.01 ml) along with positive (histamine) and negative (phosphate buffered saline) controls. all sites were examined at 20 minutes for immediate reaction, periodically over 4-6 hours and also after 24 hours. Intracutaneous tests with 55 common inhalant antigens was also done in 24 patients. In addition, skin test was also performed with the same antigens of the four *Aspergillus* species used in the study along with negative and positive controls on 15 healthy volunteers. The control group was matched, as far as possible, for age, sex and environmental background. All antigens, which were tested for their potency, were obtained from the Council of Scientific and Industrial Research Center for Biochemicals, Delhi. The tests were performed and graded as per methods already reported.[5] Only markedly positive reactions of 2+

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(wheal about 3-3.5 times the size of negative control, erythema over 20 mm) and above were considered significant. Precipitin studies for detection of antibodies against *Aspergillus* antigens using the gel double immunodiffusion technique of Ouchterlony[6] was performed in all patients.

RESULTS

The clinical and laboratory features of all 27 patients with perennial rhinitis are summarized in Table 1. An atopic background was available in 16 patients. No significant occupational history was elicited. None of the patients had a history of exposure to livestock or any source of decaying vegetable matter. Peripheral eosinophilia (more than 500 cells/mm^3) was detected in 8 patients. Routine pulmonary function tests and chest roentgenograms were normal in all patients. Two patients had radiological evidence of sinusitis.

Immediate cutaneous hypersensitivity to common aeroallergens other than *Aspergillus* antigens was observed in 13 of the 24 patients tested. Immediate cutaneous reactivity to *Aspergillus* antigens (Table 2) was observed in 7 (26%) of the 27 patients. In 3 of these 7 patients, intradermal tests with common aeroallergens did not demonstrate any significant positivity while the remaining 4 patients demonstrated cutaneous reactivity to common aeroallergens also. Thus in 3 (11%) patients, immediate hypersensitivity was limited exclusively to *Aspergillus* antigens. Late reaction was also seen in 7 (26%) patients which included one isolated late reaction against *A.flavus*. The patient with the isolated late reaction, however, demonstrated immediate cutaneous reactivity to common aeroallergens also. Cutaneous reactivity (both immediate and late) was seen more commonly with *A.flavus* antigen. None of the healthy volunteers demonstrated cutaneous reactivity to any antigens of the *Aspergillus* species.

Table 1. Clinical and Laboratory features of 27 patients with Perennial Rhinitis.

Sex	Patients
Males	18
Females	9
Age	
Range	17–40 years
Mean	26.5 years
Standard deviation	5.97
Duration of rhinitis	
Range	1–25 years
Mean	5.5 years
Standard deviation	5.60
Peripheral eosinophilia (More than 500 cells/mm^3)	8
Radiological evidence of sinusitis	2
Skin test* reactivity to common aeroallergens (24 patients)	13
Serum precipitins	1 *(A. Flavus)*

*Other than *Aspergillus* antigens.

Table 2. Skin test reactivity with *Aspergillus* antigens.

	Immediate reaction		Late reaction		Immediate and Late reaction	
	No.	(%)	No.	(%)	No.	(%)
Skin reactivity to *Aspergillus* antigens	7	(25.9)	7*	(25.9)	6	(22.2)
A. flavus	6	(22.2)	4*	(14.8)	3	(11.1)
A. fumigatus	3	(11.1)	3	(11.1)	2	(7.4)
A. niger	4	(14.8)	2	(7.4)	1	(3.7)
A. tamaril	3	(11.1)	2	(7.4)	2	(7.4)

*Includes isolated late reaction observed in one patient

Of the two patients with radiological evidence of sinusitis, one was exclusively reactive to *Aspergillus* antigens while the other patient was reactive to other aeroallergens only. Serum precipitins were not detected in either patient. Serum precipitins to *A.flavus* was detected in one patient who also had cutaneous reactivity to both *Asperillus* and other aeroallergens. Adequate clinical control was, however, achieved in our patients with topical drugs which were supplemented by oral antihistaminics and topical decongestants during exacerbations.

DISCUSSION

This study has attempted to establish the frequency of sensitization to *Aspergillus* in patients with perennial rhinitis. Immediate cutaneous reactivity to *Aspergillus* antigens was observed in 26% patients. In an earlier study on asthmatics in Cleveland and London, immediate cutaneous reactivity to *Aspergillus* was seen in 28% and 23% of patients, respectively.[2] Most human infection by *Aspergillus* is attributed to three of the four species whose antigens were used in this study, viz. *A.fumigatus, A.flavus* and *A.niger.*[7] Cutaneous reactivity in our patients was seen most commonly with *A.flavus* which also caused the isolated late cutaneous reaction.[8] Serum precipitins, detected in another patient, was also against *A.flavus* which has previously been incriminated as an important cause of *Aspergillus* sinus syndromes.[4,9,10]

These findings assume importance in light of a 7 year study of 903 college students by Hagy and Settipane,[11] wherein they observed that a positive initial skin allergy test was an important risk factor for subsequent development of allergic disorders. Three patients had an immediate hypersensitivity reaction to *Aspergillus* antigens alone. It is conceivable that hypersensitivity to *Aspergillus* may have been an important factor in the causation of perennial rhinitis in these patients. Although nasal provocation tests and serum specific IgE to *Aspergillus* antigens were not performed, it is possible that patients with skin hypersensitivity to *Aspergillus* could be at a greater risk of developing other *Aspergillus* associated hypersensitivity disorders like AAS/or ABPA at a later date, as rhinitis is an important predisposing factor for sinusitis.[12] Further studies on these aspects are warranted.

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