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Prevalence of Allergic Bronchopulmonary Aspergillosis in Patients with Bronchial Asthma

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SUMMARY **Two Hundred patients with bronchial asthma were studied to identify the prevalence of allergic bronchopulmonary aspergillosis (ABPA). The patients selected required intermittent short courses of steroids and their mean duration of illness was 12 years. Absolute eosinophil count was > 500/mm^3 in 53% of the cases. Chest X-rays showed small homogenous shadows with patchy infiltrations in 25% and fluctuating pneumonic shadows in 14% of the cases. Raised specific IgG and positive serum precipitin against *Aspergillus fumigatus* (AF) were present in 24% and 13%, respectively. Cases with radiological and immunological suspicion were further investigated for ABPA. Skin tests for Type-I and Type-III reactivity were positive with AF extract in 87% (n = 47) and 36% (n = 47) of the cases. A thorax CT of 31 patients showed central bronchiectasis in 24 cases, labeling these patients as ABPA-CB (ABPA with central bronchiectasis) and an other 7 as ABPA-S (serological positive). CT was not done in one case who, because of other positive findings, was also labeled as ABPA-S. Thus, these 32 asthmatics were found to have ABPA. Among them, there was raised specific IgG (100%) and raised specifc IgE against AF (100%), positive skin test for Type-I and Type-III reactivity (100% and 53%) against AF. There was elevated total IgE (100%, n = 29), a positive family history of asthma (63%), peripheral eosinophilia (100%) and a history of passage of brownish plugs (31%). Radiological findings suggested soft shadow with infiltration in 31% and fluctuating pneumonic shadows in 69% of cases. CT Thorax (n = 31) showed central bronchiectasis in 78% of theses patients. Based on the present data, the prevalence of ABPA in bronchial asthma patients is 16% (12% with central bronchiectasis and 4% only serologically positive). Therefore, patients should be investigated and diagnosed in an early phase of ABPA (ABPA-S) and should be treated to prevent permanent lung damage.**

Allergic bronchopulmonary aspergillosis (ABPA) was first reported in England during 1952.[1] Since then a number of cases have been diagnosed and reported from many countries.[2,3] Due to raised awareness of physicians and improved diagnostic facilities, there is a marked increase in diagnosis of ABPA. From India, only few reports are available on ABPA.[4,5,6] It is presumed that many cases are unreported. The incidence of ABPA among bronchial asthma patients has been found to vary from 3.7 to 11%[7,8] in western countries. Chetty *et al.*[9] reported ABPA in 15% of cases in a group of children with perennial asthma. In India, no data are available. Therefore, the present study was undertaken to find out the prevalence of ABPA in bronchial asthma in all age groups.

MATERIALS AND METHODS

Two hundred patients (89 males and 11 females) with bronchial asthma (reversibility > 20% in FEV_1 with 200 µg of inhaled salbutamol) were selected for the present study. The patients were aged 12-70 years (mean age 34 years). The mean duration of bronchial asthma was 12 years (4-50 years). These patients required short courses of steroids 4-6 times/year for the management of their asthma. They were all non-smokers. There was no associated history of tuberculosis, coronary artery disease, diabetes mellitus or hypertension. Detailed

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histories including family history of allergic diseases, surrounding environment, etc. were recorded. Preliminary investigation including routine blood and urine examinations, Chest X-ray, spirometry, sputum for fungal species, specific IgG against AF and serum precipitins against AF using gel diffusion technique were performed in all cases. Specific investigations like skin tests with antigen for Type-I and Type-III reactions, total IgG, and CT scan thorax were performed in suspected case of ABPA. The major criteria used for diagnosis of ABPA included: 1) history of asthma, 2) blood eosinophilia, 3) Type-I (immediate) cutaneous reactivity to AF antigen, 4) precipitating antibodies against AF antigen, 5) radiological opacities (transient or fixed), 6) specific IgG against AF, 7) specific IgE against AF and 8) CT thorax positive for proximal bronchiectasis. Other minor criteria included: 1) Type-III (Arthus) cutaneous reactivity with AF antigen, 2) sputum culture for AF, however, negative culture did not exclude ABPA, and 3) passage of brownish plugs in the sputum. In our study, for diagnosis of ABPA, at least five major criteria had to be present.

RESULTS

Two hundred patients (89 males and 11 females) with bronchial asthma were evaluated to find out the incidence of ABPA. All these cases were on bronchodilators, needing off and on short courses of steroids. The mean duration of illness was 12 years (4-52 years) and the mean age of the patients was 34 years (12-70 years). All patients had history of cough and paroxysmal breathlessness with seasonal variation. The winter was the worst season in 80% of the cases. A family history of allergy was present in 20% of the cases. Absolute eosinophil counts in these patients after de-worming consistently showed more than 500 cells/mm^3 in 53% of cases. From the cases diagnosed as ABPA, 31% showed eosinophils between 500-1,000/mm^3 and 69% showed eosinophils between 1,000-2,000/mm^3. The chest X-rays showed soft shadows with patchy infiltrations in 25% and fluctuating shadows in 14% of the cases. However, 60% of the cases had a normal chest X-ray. Cases which were diagnosed as ABPA presented with a soft shadow together with infiltration in 31% and a fluctuating shadow in 69% of the cases.

In all the cases, specific IgG against AF was estimated by ELISA and 24% were found to be positive. Serum precipitin against AF was found to be positive in 13% in all cases and all these cases were diagnosed ABPA. Sputum culture for AF was positive in 12% of the cases. There was elevated specific IgE against AF in 34 (n = 39 investigated only) cases and out of

Table 1 Laboratory data of 200 patients

	Findings	Present in/ total no.	%
1.	Bronchial asthma	200/200	100
2.	Peripheral absolute eosinophilia (per mm^3)		
	< 500	38/80	47%
	> 500	18/80	23%
3.	Radiological examination		
	- Normal	120/200	60%
	- Soft shadow with patchy infiltration	50/200	25%
	- Fluctuating pneumonic shadows	28/200	14%
4.	Specific IgG against *A. fumigatus*		
	- Present	47/200	24%
	- Absent	153/200	87%
5.	Serum precipitating antibody		
	- Present	26/200	13%
	- Absent	174/200	87%
6.	Sputum for *A fumigatus*		
	- Direct (positive)	30/200	15%
	- Culture (positive)	24/200	12%
7.	Elevated specific IgE (n = 39) (*A fumigatus*)		
	- Positive	34/39	87%
	- Negative	5/39	13%
8.	Elevated total serum IgE (n = 29)		
	- Elevated	29/29	100%
9.	Skin test *A. Fumigatus* (n = 47)		
	- Positive		
	Type-I	41/47	87%
	Type-III	17/47	36%
10.	CT Thorax (central bronchiectasis n = 31)		
	- Present	24	78%
	- Absent	7	22%

Table 2 Diagnostic profile of ABPA cases (n = 32, 14 males and 18 females)

Findings		No. of cases	%
1.	Bronchial asthma	32/32	100
2.	Family history of allergy	20/32	63
3.	History of passage of brownish mucus plugs	10/32	31
4.	Peripheral eosinophilia (per mm^3)		
	- 500-1,000	10/32	31
	- 1,000-2,000	22/32	69
5.	Radiological examination		
	- Soft shadow with infiltration	10/32	31
	- Fluctuating shadows	22/32	69
6.	Raised specific IgG against *A. fumigatus*	32/32	100
7.	Presence of serum precipitant against *A. fumigatus*	24/32	70
8.	Sputum for *A. fumigatus* (positive culture)	16/32	50
9.	Elevated total IgE (n = 29)	32/32	100
10.	Elevated total IgE (n = 29)	29/29	100
11.	Skin test (*A. fumigatus*)		
	Positive		
	- Type-I	32/32	100
	- Type-III	17-32	53
12.	CT scan (thorax) (n = 31)		
	- Central bronchiectasis	24/34	78
	- Normal	7/31	22

these 32 cases were diagnosed ABPA. In 29 cases total IgE was elevated. Skin test for Type-I reacitivity against AF was positive in 41 (n = 47) cases and Type-III reactivity was positive in 17 cases (Table 1).

Thirty-two cases which were diagnosed as ABPA were analyzed. Family history of asthma was present in 20 (63%) cases and peripheral eosinophil count was between 500-1,000 mm^3 in 69% of the cases. On radiological examination, a soft shadow with infiltration was present in 10 (31%) cases and a fluctuating pneumonic shadow was present in 22 (69%) cases.

There was raised specific IgE and specific IgG against AF in all cases. Serum precipitins against AF was present in 24 (75%) cases. There was an elevated total IgE in 29 (n = 29) cases. Skin test for Type-I reactivity was positive in 32 (100%) cases and for Type-III in 17 (53%) cases. History of passage of brownish plugs was positive in 10 (31%) cases. CT thorax showed bronchiectasis in 24 (78%) cases labeling them as ABPA-CB and 7 (22%) as ABPA-S (Table 2). CT could not be performed for one patient, but all other findings were present and he was labeled as ABPA-S. Thus, the prevalence of ABPA was 16%, out of these ABPA-CB was 12% and ABPA-S was 4%.

DISCUSSION

ABPA refers to the condition intially reported in 1952 by Hinson *et. al.*[1] characterized by recurrent roentgenographic infiltration, peripheral blood eosinophilia and sputum eosinophilia with persistent asthma. Earlier, the disease was thought to be a rarity but it has now become evident that ABPA is an important cause of significant lung damage. The diagnosis is established by using well recognized diagnostic criteria suggested by Greenberger.[12] The diagnosis should be met by the presence of all diagnostic criteria. The presence of central bronchiectasis (CB) permits the notation of ABPA-CB. If all criteria are present except detectable CB, the notation for seropositive ABPA is used.[13] In our study, the prevalence of ABPA was recorded in 16% (ABPA-CB = 12%, and ABPA-S = 4%) of all patients included in the study.

ABPA is presumed to be primarily a disease of atopic indi-

viduals with most of the reported cases occurring in the age group of 20-30 years. However, in our study 20/32 (63%) cases had a family history of allergy. All the cases were 20 to 30 years of age except one female patient who was 65 years old. In earlier reports, the incidence of ABPA among the asthmatics have been found to vary from 3.7% to 11.5%[7,8] in adults and 15% in children.[9] In our study, the prevalence of ABPA among asthmatics was 16% (ABPA-CB = 12% and ABPA-S = 4%). The incidence of ABPA in bronchial asthma with pulmonary eosinophilia varies from 28-59%.[6,14] In our study, the incidence of ABPA in bronchial asthma with pulmonary esoinophilia was 36%. Several studies showed that ABPA affects all age groups with no sex predilection,[11,15,16] but in our study, the younger age groups were more involved and there was a predilection towards females, and mostly these females were housewives and residents of rural areas.

Similar to the observations of McCartly and Pepys,[15] we also observed a higher rate of winter exacerbation of symptoms in patients with ABPA. The chest roentgenographic manifestations may be transient or persistent. The transient changes may become clear with or without corticosteroid therapy; they appear to be the result of infiltration, mucoid impaction or secretions in damaged bronchi. Permanent changes are lobar shrinkage, fibrous and central bronchiectasis. A normal chest roentgenogram does not exclude the diagnosis of ABPA. In our study, we found 24 cases having central bronchiectasis on CT scan. Forty-one of 47 (87%) cases showed Type-I reaction to AF on skin testing and 17/47 (53%) cases showed Type-III reaction. Out of these, 32 cases were diagnosed as ABPA. Earlier studies reported immediate skin reacitivity with AF in 13-38% of asthmatics and in 20% of the normal population.[17] Therefore, skin test alone is not confirmatory for ABPA. ABPA is usually associated with a marked rise of total serum IgE and IgG, which can be demonstrated by radioimmunoassay or enzyme-linked immunosorbant assay (ELISA). In our study, 29% of the cases showed a rise in total serum IgE. Twenty-four percent (n = 200) of the asthmatics had increased specific IgG and 87% (n = 39) of the cases showed a raised specific IgE against *A. fumigatus*. Out of these, 32 cases were diagnosed as ABPA.

Previous studies had reported serum precipitins against AF in 1% of the normal population[18] and 10% of the asthmatic population.[19] In the present study, serum precipitating antibodies against AF were positive in 26 of the asthmatics and out of these 24 cases were diagnosed ABPA.

All the cases in the present study experienced frequent deterioration of symptoms. This implies that worsening of symptoms and intermittent requirement of steroids in patients with bronchial asthma should be investigated for ABPA. Such early diagnosis of ABPA will help to prevent permanent lung damage. Efforts should be made to identify ABPA during the seropositive stage prior to central bronchiectasis.

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