Original Article

Allergic Bronchopulmonary Aspergillosis and Bronchial Asthma, A Forgotten Partners

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ABSTRACT

Objective: To evaluate the incidence of ABPA (Allergic Broncho Pulmanary Aspergillosis) in Asthma.
Study Design: Observational Study
Place and Duration of Study: This study was conducted at Pulmonology Department, Bolan Medical College Quetta from 2005-2010.
Materials and Methods: Forty Cases both male and female were included in this study. A detailed medical history, complete physical examination, recent posteroanteral and lateral chest X.Ray were obtained. Where ever possible previous X-Ray chest were also obtained for comparison and to see the fleeting shadows. Laboratory help included absolute eosinophil count, total serum IgE, Sputum for fungal hyphae and spirometry.
Results: Among forty (40) cases 90 % were asthmatics between 11-40 years of age. In 92 % of cases the radiological findings were fleeting in nature. 70 % were misdiagnosed and treated as pulmonary tuberculosis. All 40 case had raised (70.5 x 10^9 perlitre) absolute eosinophil count in peripheral blood. Sputum eosinophilia was detected in 77 % of cases and fungal hyphae were isolated in 47 % cases bronchospy and serum IgE levels were also abnormal but performed in only 25% cases.
Conclusion: ABPA must be considered in asthma patients having unexplained , fleeting or persistent chest radiographic shadows.
Key Words: Allergic Bronncho Pulmanry Aspergillosis (ABPA), Aspergillosis, Fumigatus.

INTRODUCTION

Aspergillus Fumigatus is a fungus that grows on dcad and decaying organic matter in the environment and whose spores are present ubiquitously in the air[1]. Allergic bronchopulmanary aspergillosis is a hypersensitivity lung disease, caused predominantly by the ubiquitous fungus aspergillosis fumigatus[2]. Aspergillus Fumigatus is associated with a number of pulmonary conditions including ABPA, mycetoma, invasive aspergillosis, extrinsic allergic alveolitis and bronchial asthma[3]. Proximal bronchiectasts is also a very common sequalae of ABPA. The disorder needs to be detected before bronchiectasis has developed because the occurrence of bronchiectasis is associated with poorer out comes[4].Diagnosis of ABPA is usually difficult and majority of the patients are misdiagnosed as pulmonary tuberculosis due to suggestive symptoms of cough, sputum, fever, breathlessness and fleeting shadows on chest radiograph. Due to lack of proper diagnostic laboratory facilities for fungal infections these patients end up having multiple courses of anti-tuberculous therapy and antibiotics by different doctors without adequate clinical and radiological improvement.

This study reveals forty cases of ABPA seen over a period of five years (2005-2010) in a personal series. The purpose of this study is to evaluate the pattern of this relatively un-common problem in our clinical practice and also to provide guidelines for the proper diagnosis and management.

MATERIALS AND METHODS

The majority of the patients with the suspected diagnosis of ABPA were picked from the Department of Chest Medicine, Bolan Medical collage Quetta. A few patients were also included from a private clinic. A detailed medical history was taken, a complete physical examination was performed, radiological and laboratory investigations were obtained. Where-ever possible previous X-ray chest were also obtained for comparison and to see fleeting shadows. Laboratory investigations included TLC, DLC, ESR, absolute eosinophil count, total serum IgE, sputum for fungal hyphae and spirometry.

All the patients were treated with oral steroids.Majority of them received oral prednisolone 40 mg daily for 4 to 6 weeks. Response to treatment was assessed on the basis of clinical improvement, radiological clearance and fall in absolute eosinophil count in peripheral blood.

RESULTS

A total of 40 cases of ABPA were seen over a period of five years. The age and sex distribution is shown in Table 1 and 2. Overall the ABPA was found to be more common in females and 90% of the patients were in the age group 11 to 40 years. Majority of the patients presented with marked overlap of multiple symptoms like cough, sputum, breathlessness, wheeze and fever. Characteristic mucus plugs which are hard, rubbery and yellow to brown lumps were seen in 50% cases. Haemoptysis and chest pain were relatively less common (Table 3) Past medical history revealed bronchial asthma in 36 cases (90%) and atopy in

31 cases (77.5%) whereas 28 cases (70%) were misdiagnosed as pulmonary tuberculosis and received un-necessary single or multiple courses of anti-tuberculous therapy. Clinical examination of respiratory system revealed features of asthma (90%) consolidation (32.5%) bronchiectasis (22%) and collapse / fibrosis (10%).

Table No.1: Age Distribution in 40 Cases

Age group	Number	Percentage
0-10	Nil	0%
11-20	9	22.5%
21-30	17	42.5%
31-40	10	25%
41-50	3	7.5%
51-60	Nil	0%
61-70	1	2.5%
Total	**40**	**100%**

Table No.2: Sex Distribution in 40 Cases

Sex	Number	Percentage
Male	17	42.5%
Female	23	57.5%
Total	**40**	**100%**

Table No.3: Presenting Complaints in 40 Cases

Symptom	Number	Percentage
Cough	40	100%
Sputum	37	92.5%
Shortness of Breath	34	85%
Wheeze	33	82.5%
Fever	33	82.5%
Haemoptysis	9	22.5%
Chest Pain	5	12.5%

Table No.4: Radiological Presentation in 40 Cases

Nature	Number	Percentage
Consolidation	27	67.5%
Infiltrate	26	65%
Bronchiectasis	23	57.5%
Fibrosis / Collapse	11	27.5%
Fleeting Shadows	37	92.5%

Features on chest radiograph included multiple abnormalities with significant overlap in all three radiological zones (Table 4 and 5). Thirty seven cases (92.5%) showed characteristic fleeting shadows which are hallmark of ABPA. In 14 cases (35%) lesions were seen in perihailar area. Blood examination showed raised TLC in 22 cases (55%) but absolute eosinophil count was raised in all 40 cases indicating eosinophils replacing other differential leucocytes (Table 6). Spirometry was performed in all cases and 31 cases (77.5%) revealed features of obstructive airway pattern. High sputum eosinophil count was seen in 31 cases (77.5%) but the yield of sputum for fungal hyphae was relatively low (47.5%). Bronchoscopy was performed in 10 cases (25%) showing hyperemic, oedematous mucosa and rubbery brownish mucous plugs causing bronchial obstruction in lobar and segmental bronchi. Serum IgE levels were checked in only 10 cases (25%) and was found to raised.

Table No.5: Distribution of Radiological Sites (Zones) in Cases

Zones	Cases	Percentage
Single zone	5	12.5%
Double zone	14	35.0%
Triple zone	21	52.5%
Total	40	100%

Table No.6: Range of Absolute Eosinophil count

Range	No. of cases	Percentage
500-1000	22	55%
1001-2000	14	35%
2001-3000	1	2.5%
3001-4000	2	5%
4001-5000	1	2.5%
Total	40	100%

All 40 cases were treated with oral prednisolone 40 mg daily in addition to symptomatic therapy for asthma and superadded infection (Table 7). Total duration of daily treatment with oral prednisolone was 4-6 weeks in 33 cases (82.3%) after initial 4 weeks of daily 40 mg prednisolone dose was tapered and stopped in the following 2 weeks. Two cases failed to tolerate oral prednisolone more than 2-3 weeks whereas in five cases treatment has to be continued for 7-10 weeks. Those patients who received prednisolone for less than 4 weeks showed significant clinical improvement. This was confirmed by clearance of radiological shadows in repeat chest radiograph and fall in absolute eosinophil count to normal level in peripheral blood film.

Table No.7: Treatment in 40 Cases

Drug	Number	Percentage
Steroids(oral)	40	100%
B-Agonist	33	82.5%
Theophyline	6	15%
Inhaled Steroids	20	50%
Antibiotics	12	30%

During follow-up 10 cases (25%) had relapse. Majority of these developed relapse between 6-12 months. Three patients had 2-3 episodes of relapse but all were treated successfully with 4-6 weeks duration of oral prednisolone. None of cases required long term maintenance steroids.

DISCUSSION

Aspergillosis in one the Ist mycosis to be recognized in humans[5]. aspergillus fumigatus is the most frequently implicated pathogen causing ABPA and other lung diseases[6]. ABPA, Ist described in 1952 by Hinson and Coworkers is caused by hypersensitivity and immunological reaction to A. Fumigatus involving the bronchial wall and peripheral part of the lung [7]. in vast majority of cases ABPA is associated with bronchial

asthma but it can occur in non-asthmatic patients[8-9]. The identification of allergic fungal sinusitis (AFS) is much more recent than that of allergic broncho pulmonary aspergillosis (ABPA) and may still be incomplete and controversial[10].In our study 36 cases (90%) were asthmatics and 31 cases (77.5%) had history of atopy. Another study by Bromley and Donaldson[11] has suggested that asthmatic lung has an environment which is more conducive to the adherence and persistence of A. Fumigatus spores than the normal lung. ABPA usually develops in atopic individuals in their 20s – 30s and relatively more common in females[12]. In our study 57.5% cases were females and 90% of the patients were in the age group 11 to 40 years.

Diagnostic criteria of ABPA include follows[13]

- Asthma (in the majority cases).
- Chest radiographic abnormalities.
- Elevated total serum IgE.
- Fungal hyphae of A. Fumigatus in sputum.
- Positive Skin test and precipitating antibodies.

Radiographic changes in ABPA may be transient or permanent[14]. transient changes are fleeting in the form of diffuse pulmonary infiltrates, lobar or segmental collapse and fluffy sonsolidations in any part of the lungs. Permanent radiographic abnormalities include loss of lung volume, fibrosis and bronchiectasis particularly in upper lobes. Similar changes are also seen in pulmonary tuberculosis causing major confusion in the diagnosis.

In our study 28 cases (70%) were misdiagnosed as pulmonary tuberculosis, out of these 14 cases were given single course, 10 had two curses and 4 cases had three courses of un-necessary anti-tuberculous therapy.

In addition to radiological findings, absolute eosinophil count was found very useful in the diagnosis as all the cases had raised count (Table 6). Sputum containing fungal hyphae is produced intermittently by patients in ABPA. In our study approximately 50% cases were positive for fungal hyphae. Total serum IgE levels in ABPA are generally markedly above the normal range and higher than those found in uncomplicated asthma[15]. we were able to perform total serum IgE levels in only 25% cases. Bronchoscopy can be useful both for diagnostic and therapeutic purpose particularly for removal of mucus plugs in lobar and segmental collapse. Positive skin test and serum precipitating antibodies to A. Fumigatus are found in majority of cases but due to lack of availability were not performed. The mainstay of treatment of acute exacerbation in ABPA is oral corticosteroids (Prednisolone 40-60 mg daily) and patients having recurrent episodes may require maintenance dose of 10 mg daily on long term basis [16,17]. transient radiographic abnormalities usually clear within 4-6 weeks, whereas permanent radiographic changes may clear partially. In our study more than 80% cases received oral prednisolone 40 mg dose for 4-6 weeks and showed good response. The optimal control of asthma should be achieved with inhaled corticosteroids and bronchodilators. Inhaled coricosteroids do not prevent pulmonary infiltrates bud do not appear to encourage fungal growth within lung[18].Early recognition allows treatment with corticosterorids, which are effective but may be required indefinitely[19]. The trial of treatment with oral antifungal agents like ketoconazole and imidazole are in progress. Those can reduce concentration of specific antibodies with improvement in asthmatic symptoms but prolonged treatment and potential toxicity limits their use[20].

CONCULUSION

ABPA is relatively rare but serious complication of bronchial asthma. The disease usually follows chronic course with recurrent episodes of pulmonary infiltrates and lobar or segmental collapse. The aim of our study was to establish a diagnostic and therapeutic criteria for cases of ABPA. Although similar radiographic abnormalities can be seen in sarcoidosis, allergic alveolitis and cystic fibrosis but in our community pulmonary tuberculosis is the main differential diagnosis. We hope that by establishing appropriate early diagnosis of ABPA, majority of the patients can be saved from un-necessary anti-tuberculous therapy.

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CORRIGENDUM

It is to clarify that the department of Dr. Zafarullah Khan at Sr.No.2 in the article "Diurnal variations in the levels of Progesterone during late pregnancy" appeared in our Journal Medical Forum Monthly, October, 2011 (page 28) may be read as Endocrinology instead of Entomology.

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