Clinical Experience with Allergic Bronchopulmonary aspergillosis in a tertiary care hospital.

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Abstract

Background: Allergic bronchopulmonary aspergillosis (ABPA) is hypersensitivity reaction to Aspergillus antigen. It occurs in patients with asthma and cystic fibrosis (CF) and manifest as fever and pulmonary infiltrates unresponsive to antibiotics.

Objective: Objective of the present study was to analyze clinical experience with ABPA in tertiary care center.

Methodology: It is an observational study. Patients data with diagnosis of ABPA from AKUH (agha khan university hospital) admitted in 2016 were collected retrospectively. Patients who fulfilled the ISHAM (International Society for Human and Animal Mycology) criteria were included. History, disease stage, radiological findings, Spirometry, treatment and outcome were recorded on predefined questionnaire. SPSS V21 was used for data analysis.

Results: Out of 120 patients, 64 fulfilled the criteria for ABPA. Mean duration of ABPA was 4 years. 25% were misdiagnosed as pulmonary Tuberculosis. Mean Eosinophil count was 1111/mm². Serum IgE level was above 2000 IU in 88% of patients. Mean age of patients were 32±12 years. 49% of them were males. 22% were having acute flare, 33% were having remission, 22% were steroid dependent and 1% had fibrotic lung disease. Most common symptoms were cough 88%, fever 66% and wheeze 56%. 55% had central bronchiectasis on HRCT. 28% had aspergillus fumigatus, 18% aspergillus flavus, 20% pseudomonas aerogenosa and 11% had streptococcus pneumonia on sputum culture.

Conclusion: ABPA is commonly misdiagnosed as pulmonary TB in high burden TB country. Early diagnosis and appropriate treatment can prevent the structural damage to the lungs.

Key words: ABPA; AKUH; Pulmonary TB
Introduction

Aspergillus is a fungus of clinical significance found in every part of the world. It has multiple species i.e. A. fumigatus, A. flavus, A. Niger, A. terreus. Inhalation of aspergillus conidia is very common and only a minor subset of those develops disease. The clinical feature largely depends on host immune response. Aspergillus fumigatus is the most common species implicated in all pulmonary syndromes. Aspergillus flavus causes rhinosinusitis, postoperative aspergillosis and fungal keratitis. A. Niger is more commonly found as colonizer but sometime it causes bronchitis. A. terreus has been implicated for invasive aspergillosis and is Amphotericin B resistant.

Aspergillus causes a spectrum of clinical syndromes in human host depending on the host immune response to aspergillosis. Clinical syndromes of pulmonary Aspergillus infections are: Invasive aspergillosis, chronic pulmonary aspergillosis, Allergic bronchopulmonary aspergillosis (ABPA) and EAA (extrinsic allergic alveolitis) secondary to aspergillosis and aspergilloma. Invasive aspergillosis is more likely seen in immunocompromised hosts like transplant recipients, patient with chemotherapy and long term steroid users. Chronic pulmonary aspergillosis (CPA) is a more indolent disease presenting with prolonged and relapsing cough, dyspnea and weight loss. It usually affects with underlying lung diseases like patients with chronic obstructive pulmonary disease. Aspergilloma are round fungal balls with mucus and cellular debris that form in lung cavities. There is 15-20% risk of developing aspergilloma in cavity of >2cm diameter and most serious complication is haemoptysis.

Allergic Bronchopulmonary aspergillosis (ABPA) is a hypersensitive reaction to aspergillus antigen. It occurs in persons with asthma and cystic fibrosis. ABPA was first described in 1952 by Hinson, Moon and Plummer. It is one of the causes of asthma exacerbation. In normal humans, inhaled spores are cleared from the airways but defective clearance in asthma and cystic fibrosis patients lead to germination of these spores into hyphae and then those lead to formation of pro inflammatory markers. There appear to be a genetic predisposition to developing ABPA, which is supported by work showing a familial occurrence of 4.9%. It is one of the underrecognised conditions but failure to diagnosis can lead to lung fibrosis and bronchiectasis.

A first diagnostic criterion was purposed by Rosenberg, Patterson, and colleagues in Chicago in 1977. Diagnostic criteria has been revised by International society for Human and animal mycology recently. To diagnose there should be underlying predisposing condition like Asthma or Cystic fibrosis. Specific Aspergillus IgE should be positive and Total IgE level should be more than 1000IU/ml. Then 2 or more than 2 of the following should be positive i.e. Aspergillus skin test, eosinophil > 500, IgG against Aspergillus or aspergillus precipitins should be positive. And on High Resolution CT (HRCT) if bronchiectasis is present than it is called ABPA-B and if HRCT is normal then it is called as ABPA-S. ABPA x-ray and symptoms mimics that of tuberculosis. A high index of suspicion is always required to diagnose this disease. In a TB endemic country, there is high chance of mistreating ABPA as Tuberculosis or recurrent bacterial pneumonia. In this study, we have presented our experience with this disease in our tertiary care center and have also shown how many of these patients were misdiagnosed initially.

Methodology

It is an observational study. Ethical review was sought from our hospital ethical committee. All Patients who presented in Aga Khan University Hospital, Pulmonology Unit with principle diagnosis of ABPA were sought from Electronic health record from January to December 2016. To protect identity, no identifiable data were documented from each case. Modified International Society for Human and Animal Mycology (ISHAM) criteria was used to diagnose ABPA. All patients who full filled these criteria were included in this study. Modified ISHAM criteria used were as follows:

1. Predisposing Condition. Asthma, Cystic Fibrosis
2. Essential Criteria
   a. Specific IgE against A. fumigatus
   b. Serum total IgE >1000
3. Supporting criteria (≥ 2)
   a. Eosinophil count >500
   b. Increased IgG antibody against Aspergillus fumigatus
   c. Aspergillus fumigatus precipitins positive
   d. Consistent radiologic opacities

Those entire patients who did not fullfil these criteria were excluded. Patient who were already on treatment from other centers, were excluded as we did not have their diagnosis data. History of each patient, stage of disease, radiological findings, spirometry findings, treatment given and outcome were recorded on predefined questionnaire.

Data were recorded and analyzed by SPSS version 21. Frequencies and percentages were calculated for

PJCM 2019; 25 (3) 115
Results

Total of 120 patients presented to Pulmonology Unit in year 2016. 64 met our inclusion criteria. Mean age of patients was 32±12 years. Out of 64, 31 (49%) were males and 33 (51%) were female. 60 (94%) were nonsmokers, 2(3%) were current smokers, 2(3%) were reformed smokers. 3(5%) had biomass exposure. None of our patient has ABPA family history. Bird exposure was positive in only 4(6%). 25% patients were initially misdiagnosed and mistreated as pulmonary tuberculosis before being referred to us. Mean eosinophilic count was 1111/mm2. Two of our patient had IgE level<1000. And seven patients (10%) had eosinophil count < 500. Four patients has positive beta glucan test. 22% of our patients had no asthma history. Comorbidities are shown in (Table 1).

Most common symptom among all was cough seen in 83% of patient. Common symptom of ABPA is shown in (Figure 1). 33% of our patients were in remission. Only 1 patient had developed fibrotic lung disease. Stages of ABPA are shown in (Figure 2). Chest x-ray most common finding was bilateral infiltrates 47% and fleeting infiltrates 61% (Table 2). HRCT showed Central bronchiectasis in 52% of patient and Mucus plugging in 65% (Table 3). 22 patients had Spirometry data. Mean FEV1/FVC ratio was 67.5±9. Figure 3 is showing histogram of FEV1/FVC ratio.

All patients were given steroids. 20% of our patient had steroid dependent disease. 70% of our patients were on Itraconazole. Only 20% has Influenza and Pneumococcal vaccination done. Bronchoscopy was done in 9 (14%) patients. BAL culture data from this subset of patient Sputum culture data showed 28% had aspergillus fumigatus, 18% had aspergillus flavus, 20% had pseudomonas aerogenosa and 11% had streptococcus pneumonae.
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Discussion

ABPA is one of the important diseases that remained underdiagnosed and primary physicians need more awareness regarding this disease. We have reviewed prior ABPA cases. ABPA is primarily seen in asthmatics but sometime can be seen in non-asthmatics also. In two prior studies, total of 12 patients came with no asthma history. While in our study 7 patient had no asthma history. One study has shown allergens other than Aspergillus but in our study no other mycosis was found. One of the areas of controversy is cutoff values of IgE and Eosinophil counts. Some center are using IgE>1000 as cutoff, while other as >417IU/ml. In our series, two patient had IgE<1000. Serial IgE monitoring has been recommended by many authors to monitor disease control.

Central bronchiectasis is the most common finding in prior studies while in our series it was second most common presentation. First most common presentation was mucus plugging that was seen in 65% patients while central bronchiectasis was seen in 52%. Pleural effusion has also been seen by some authors although relatively rare. In our series, no patient came with pleural effusion on x-ray. On other hand 2 patients presented with pneumothoraces. Pneumothorax secondary to ABPA is very rare. We were able to find only two prior cases with pneumothorax.

Many of clinical features of ABPA are similar to Tuberculosis like weight loss, fever, cough and sputum production with infiltrates on chest x-ray. Therefore, lot of patient with ABPA is misdiagnosed with Tuberculosis in tuberculosis high burden areas. It has been reported up to 29% in one study and 38.4% in second study that ABPA patient were misdiagnosed as tuberculosis. In our study, 25%...
patients were initially has been treated as tuberculosis.

**Conclusion**

ABPA has variable clinical, radiological patterns. Many of the patients with this disease are initially misdiagnosed as Pulmonary Tuberculosis. Threshold for ABPA diagnosis should be low as it's not so rare we think and every effort should be made to avoid misdiagnosis of ABPA which is very important for its early treatment and control and to avoid its complications.

**References**

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