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Clinical, radiological, and immunological assessment of allergic bronchopulmonary aspergillosis

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Abstract

INTRODUCTION: Allergic bronchopulmonary aspergillosis (ABPA) is an immunologically mediated lung disease, predominantly in patients with asthma and is caused by hypersensitivity to colonized dimorphic fungus *Aspergillus*, commonly *Aspergillus fumigatus*. Early diagnosis with recognition and treatment of chest radiographic infiltrates appears to prevent progression to end stage fibrosis. Many cases are mistreated as pulmonary tuberculosis or recurrent pneumonia and are deferred for specific treatment of ABPA. **AIM AND OBJECTIVES:** This study aims to know the clinical, radiological, and immunological profile of patients diagnosed with ABPA reporting to the Institute of Respiratory Disease, SMS College, Jaipur and Mahatma Gandhi Medical College, Jaipur. **MATERIALS AND METHODS:** Hospital-based prospective, observational, cross-sectional study was conducted in 48 Patients having history of bronchial asthma, pulmonary infiltrate/shadows on chest X-ray were subjected to routine investigations, immunological tests including modified skin prick test with specific IgE against *A. fumigatus* and specific precipitins against *A. fumigatus*. **RESULT:** In this study, maximum predominance with age group of 21–40 years irrespective of sex pattern. Maximum patients were having bronchial asthma of 2–10 years duration. Cough, breathlessness, and wheezing were main clinical features. In 80% cases, total eosinophilic counts were more than 1000. 58.4% sputum were fungal culture positive, maximum for *A. fumigatus*. All cases showed modified skin prick test positivity against *A. fumigatus*. Maximum patients high-resolution computed tomography chest had central bronchiectasis. 37% cases had raised total serum IgE (range 1000–5000). Specific IgE against *A. fumigatus* were positive in 24 patients. 87.5% patients were positive for specific precipitins. **CONCLUSION:** In this study, ABPA was found more commonly in people with chronic asthma of productive age group, i.e., 20–40 years and farmers by occupation. Most of the people were diagnosed as having pulmonary tuberculosis and deferred specific treatment for a long time. More knowledge about ABPA to physicians could possibly cut short the time between suffering, diagnosis, and proper treatment of these patients.

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Full Text

Introduction

Aspergillus is a saprophytic ubiquitous fungi associated with respiratory diseases; spectrum varies from colonization of the respiratory tract to rapidly invasive disseminated disease. It can be broadly classified as allergic bronchopulmonary aspergillosis (ABPA), aspergilloma, and invasive aspergillosis.

ABPA is an immunologically mediated lung disease, predominantly in patients with asthma and is caused by hypersensitivity to colonized dimorphic fungus *Aspergillus*, commonly *Aspergillus fumigatus* (about 95%).^[1] Some other species of *Aspergillus* namely *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus terreus*, *Aspergillus oryzae*, and *Aspergillus tamari* have been reported to be causing ABPA. It is a chronic relapsing disorder characterized clinically from mild asthma to end-stage fibrotic lung disease. The disease is not transmitted from animals to human beings and also not from one person to the other.

Early and aggressive treatment of ABPA is crucial for preventing serious sequelae of central bronchiectasis, pulmonary fibrosis, severe impairment in lung function and cor pulmonale. Many cases are mistreated as pulmonary tuberculosis or recurrent pneumonia and are deferred for specific treatment of ABPA.

Aim and objectives

To know the clinical, radiological, and immunological profile of patients diagnosed with ABPA reporting to the Institute of respiratory disease, SMS College, Jaipur and Mahatma Gandhi Medical College.

Materials and Methods

Study design

This was a prospective, observational, cross-sectional study, over a period of 3 years, carried out in the Department of Pulmonary Medicine at Institute of Respiratory Diseases, SMS Medical College and Mahatma Gandhi Medical College, Jaipur.

Study population

Forty-eight adult cases of ABPA, belonging to both the genders, attending the department of pulmonary medicine during the study, were included after confirming to the inclusion and exclusion criterion.

Inclusion criterion

Adult patients of both genders diagnosed as ABPA, attending the outpatient and inpatient departments of pulmonary medicine, were included in the study.

Exclusion criterion

HIV positive, active pulmonary tuberculosis, and unwilling patients were excluded from our study.

Study protocol

Approval of the institutional ethics committee was obtained and a written informed consent was taken from every patient included in this study. A detailed history and clinical examination (including general, respiratory, and other systemic examinations) findings were recorded for each patient. Chest radiography and other relevant investigations were carried out in each patient. Depending on the results of the initial clinical evaluation, patients having a history of asthma underwent detailed investigations such as complete blood count, pulmonary function test, sputum acid fast bacilli smear and culture, HIV status, high-resolution computed tomography (HRCT) thorax, modified skin prick test, and total IgE. Cases having total IgE more than 1000 IU/ml or positive skin prick test were further subjected to specific IgE to *A. fumigatus*. Forty-eight cases were having specific IgE to *A. fumigatus* >0.35 kUA/L and were diagnosed as ABPA.[2] Modified skin prick test performed using lancet by raising the skin at 45 degree and specific IgE to *A. fumigatus* was done by immunocap method.

Results

Forty-eight diagnosed cases of ABPA were included, out of these 28 were male (58.3%) and 20 were female (41.7%) with maximum (66%) predominance in the age group of 21–40 years irrespective of sex pattern. There was a very distinct pattern observed in this study that most commonly farming predispose these patients to probable heavy burden of *Aspergillus* spores (66%) followed by home workers and laborers (12%). Cough, breathlessness, and wheezing were main predominant symptoms present in all cases (100%) followed by fever in 83%, expectoration in 79.2%, brownish plugs in sputum 52%, chest pain in 33.3%, hemoptysis and clubbing in 31% of the cases [Table 1]. At the time of presentation, maximum patients, i.e., (83.4%) were having bronchial asthma of 2–10 years duration which indicated chronicity of the disease. Thirty-eight (79.2%) patients were having associated allergic rhinitis, 22 (45.8%) patients had spring catarrh and 2 (4.1%) with skin allergy signifying that majority of these patients were having allergy of other systems also along with bronchial asthma. Majority of the patients (70%) were having a history of consumption of Antitubercular therapy (ATT) once or for many times at the time of presentation. Thirty-three of patients were having ATT for duration of 1–2 years and 15% of patients having history of multiple course of antibiotics for recurrent pneumonia. Consumption of ATT and multiple course of antibiotics is the main factor behind the late arrival of these patients to us for specific diagnosis. Total eosinophilic counts were <500 in around 40% of patients as patients may be either on steroids or concealed the history of steroid intake. In our study, five patients had total IgE between 800 and 900 IU/ml, rest all above 1000 IU/ml and only 8% patients had more than 10,000 IU/ml [Table 2]. Sputum of all the patients were subjected for fungal culture, only 29% sputum were culture positive. The most common fungus found was *A. fumigatus*. Four patients had negative modified skin prick test [Table 3]. ABPA-S was found in only 2% of patients after confirmation by HRCT. Thirty-six (87.5%) cases had central bronchiectasis which is highly sensitive and specific technique for diagnosis of bronchiectasis. 47% of patients had consolidation on HRCT and 14% of patients had high attenuation mucus [Table 4]. Although mucoid impaction is generally hypodense, high-attenuation mucus (defined as mucus visually denser than paraspinal skeletal muscle) is a pathognomonic feature of ABPA. Hyperattenuating mucoid impaction has a specificity of 100% (sensitivity 19%–32%), thus making it a good “rule-in” test.[3],[4]{Table 1}{Table 2}{Table 3}{Table 4}

Discussion

A. fumigatus spores are 2–4 μ in diameter, and when inhaled in patients with impaired mucous clearance and airway obstruction, the spores may germinate and release an array of antigens, resulting in a complex immune response by the host as it gives both Type I (immediate type) and Type III (Arthus type immune complex mediated).[5] ABPA basically is an allergic (immunological) phenomenon to spores of *A. fumigatus* and a chronic relapsing disorder presenting with bronchial asthma predominantly or worsening of preexisting asthma (poor response

to inhaled steroids and bronchodilators), peripheral eosinophilia, transient pulmonary infiltrates/migratory shadows or central bronchiectasis on chest skiagram.

There are five stages of ABPA.[6] These stages are not the sequential phases of the disease as patient may present in any stage of the disease and even with end stage pulmonary fibrosis.

Acute stage: Patients are symptomatic, presenting with sputum production and symptoms of asthma. Corticosteroids are indicated to achieve remission
Remission stage: The total serum IgE declines and stabilizes and radiographic infiltrates disappear after 6 months of corticosteroids. Remissions may be permanent, but an ABPA exacerbation can occur after a remission of many years
Exacerbation stage: Occurs when there is a new chest roentgenographic infiltrate unexplained by other causes, associated with doubling of total IgE. The exacerbation may present with constitutional symptoms such as increase in dyspnea, wheezing, fever, myalgias, and sputum production in a patient but at times it may not be associated with constitutional symptoms despite large areas of roentgenographic consolidation. Management requires corticosteroids for remission
Corticosteroid-dependent: Patients become symptomatic when repeated attempts are made to taper corticosteroids used for Stage I or III and may present as uncontrolled asthma
Fibrotic: Repeated episodes of ABPA have cause end-stage fibrotic lung disease.

The prevalence of ABPA is still not known exactly due to variation in the use of diagnostic criterion.[2],[7],[8],[9],[10] Conventionally, the prevalence of ABPA is believed to be 1%–2% in patients with asthma and 2%–15% in patients with cystic fibrosis.[11] The condition is being increasingly recognized and the estimated prevalence rates in recent publications have been reported ranging from 5.9% to 20.5% for ABPA.[12],[13] The diagnosis of ABPA is based on a composite criteria incorporating clinical, radiological, and immunological findings.

Clinical spectrum of ABPA varies from asymptomatic to extensive disease present as respiratory failure. Our study cases presented predominantly with breathlessness, cough, and wheezing. Other clinical features were hemoptysis and brownish plug in expectoration due to thick mucus plug in around 30% of cases, supported by Shah and Panjabi study 2016.[14] which reviewed 113 patients with ABPA and recorded cough in 99%, breathlessness in 99%, expectoration in 98%, wheezing in 97%, and hemoptysis in 41%. Expectoration of sputum plugs was reported by 37% of the patients. Almost similar results were reported by Kumar and Goel study in 2013.[15] Kumar and Gaur[16] found cough and breathlessness in all the patients with 31% of patients giving history of brownish plugs in sputum. Hence, symptoms of asthma and wheeze should raise suspicion of ABPA. Bronchial asthma may also present with other clinical allergic atopic conditions which manifest at early age.

Laboratory findings

Total eosinophil count was considered as major criterion in Rosenberg criterion[7] but in our study around 40% of patients had normal eosinophil count. Normal eosinophil count during exacerbation may be due to intake of steroid. Whereas serum IgE level decreases on prolonged therapy of steroids (6–8 weeks) not on short therapy.[14] Thus, the total peripheral eosinophil is considered in minor and serum IgE in the obligatory criterion in recent criterion. In our study, we observed modified skin prick test positivity against *A. fumigatus* in around 90% of the patients. These observations are well supported by other studies Patterson et al.,[15] Greenberger,[1] Bedi[16] and Kumar and Gaur,[17] Guleria et al.[18] who reported immediate skin test positivity against *A. fumigatus* in all the patients (100%) of ABPA diagnosed by Patterson criterion. This is one of the most important and simplest available major criteria to confirm the diagnosis of ABPA in the suspected patients and many of the scientists took it as inclusion criteria for patients in studies of ABPA.

Radiological findings

HRCT of thorax is the preferred radiologic investigation in ABPA as it allows better assessment of the distribution of bronchiectasis and detects other abnormalities such as hyperattenuated mass that are not apparent on the chest radiograph. In our study, radiologically maximum patients showed central bronchiectasis followed by consolidation picture. Whereas reverse pattern was seen in Shah and Panjabi in 2016 study.[19] This depends on the time of presentation as bronchiectasis can be because of consolidation. Next predominant picture was fibrocavitary lesion which can be at initial presentation and becomes very difficult to distinguish it from tubercular origin. Fibrocavitary picture can also present at end stage due to misdiagnosis and inadequate treatment. Mucoïd impaction was also an observed dominant feature and seen as toothpaste, gloved finger appearance. It can be transitory also, as secretions may clear with or without therapy. We also observed 2% of cases had normal chest skiagram. Hence, all asthmatic patients should undergo screening for ABPA with *A. fumigatus*-specific IgE.[10]

Conclusion

Even with much literature available on subject and diagnosis reporting of ABPA is very poor mainly because of less acquaintance to the disease pattern amongst physicians. In this study, ABPA was found more commonly in people with chronic asthma of productive age group, i.e., 20–40 years and farmers by occupation. Most of the people were diagnosed as having pulmonary tuberculosis and deferred specific treatment for a long time. Continuous pouring of ABPA patients to the higher centers after suffering from long illness and more knowledge about ABPA conferred by these type of studies to physicians could possibly cut short the time between suffering, diagnosis and proper treatment of these patients. Patients of chronic bronchial asthma should be investigated further for ABPA.

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Conflicts of interest

There are no conflicts of interest.

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