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Spectrum of Allergic Bronchopulmonary Aspergillosis: Insights from a Case Series Emphasizing Clinical and Immunoradiological Heterogeneity

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Abstract: ***Allergic bronchopulmonary aspergillosis (ABPA) is an immunologically mediated lung disease caused by hypersensitivity to fungi, usually aspergillus fumigatus colonizing the airways of patients with underlying chronic lung diseases most commonly bronchial asthma and cystic fibrosis. Despite improved awareness and understanding of this disease, it still remains underdiagnosed and, in some cases, misdiagnosed as tuberculosis, as noted in our case series; to the detriment of patients who can progress irrevocably towards bronchiectasis, fibrosis, chronic airflow limitation with complications of pulmonary hypertension (PH) and respiratory failure (RF) if not treated early and adequately. This case series of 30 patients fulfilling revised ISHAM (International Society for Human and Animal Mycology) criteria for ABPA highlights the heterogenicity in clinical presentation, the need for definitive diagnosis using radiological criteria and biomarkers, and prompt treatment with anti-inflammatory and anti-fungal agents. Our case series emphasizes the need to vigorously investigate every patient with moderate to severe obstructive airway disease (OAD) for ABPA since early detection will control and reduce exacerbations of OAD, thus improving quality of life and prevent progression to bronchiectasis and complications like PH and RF. Research Question: What is the prevalence and clinical–radiological and immunological profile of ABPA among patients admitted with chronic airway diseases in a tertiary care center?***

Keywords: Asthma, ABPA, Bronchiectasis, IgE, Absolute eosinophil count

1. Introduction

Allergic Bronchopulmonary Aspergillosis (ABPA) is a hypersensitivity reaction to Aspergillus colonisation in the airways of patients with underlying chronic lung disease, leading to chronic airway inflammation due to an exaggerated type 2 immune response, eosinophilic inflammation and elevated IgE levels, resulting in bronchospasm, mucus plugging, difficult-to-treat OAD or recurrent exacerbations of OAD and progressive bronchiectasis. It occurs in about 10% of asthma patients but countries like India and Japan report a higher prevalence.[1] The term ABPA is used when there is colonization , but not an invasive infection, due to Aspergillus fumigatus resulting in a maladaptive immune response ; commonly in patients of bronchial asthma and cystic fibrosis, though it can occur in other chronic underlying lung conditions like bronchiectasis and chronic obstructive pulmonary disease (COPD) and rarely can occur in the absence of any predisposing condition. If an ABPA like syndrome is caused by other aspergillus species, then the term allergic bronchopulmonary mycosis is used. ABPA diagnosis has always been formulated by criteria sets which have evolved over time [2,3,4,5,6] as a constellation of clinical, serological and radiographic criteria need to be fulfilled for diagnosis. The need for early diagnosis and treatment cannot be over emphasized, as otherwise it progresses irrevocably towards fibrosis and end-stage lung disease, with complications of pulmonary hypertension and respiratory failure. In this series all patients admitted to our tertiary care center with moderate to severe asthma, and patients diagnosed with COPD and bronchiectasis with AEC>500cells/cmm were investigated for ABPA. We studied their clinical, radiological and immunological profile, with a view to highlight its varied presentations and emphasize the need for a high level of suspicion of ABPA in all cases of obstructive lung disease.

2. Methods

Data of Thirty patients with ABPA, diagnosed using the revised ISHAM criteria[2], in the Department of Pulmonary Medicine of our tertiary care hospital over a duration of 7 months, was analysed.

Patients demographic data, presenting complaints, underlying chronic lung disease if any, radiological abnormalities in Chest Xray and HRCT thorax scan, serological markers like peripheral absolute eosinophil count and serum IgE including quantitative *A. fumigatus*–specific IgE and skin prick test (SPT) to aspergillus antigens were studied.

A total serum IgE > 500 IU/mL was considered supportive of diagnosis.

A specific IgE level > 0.35 kUA/L was considered positive for sensitization.

Statistical Analysis

Descriptive statistics were used. Continuous variables are presented as mean ± SD. Categorical variables are presented as percentages.

3. Results

Demographic and Clinical findings

- Of the 30 patients studied, 12 were females and 18 males; with mean age of presentation being 39 years (18 - 63 years).

- 32 patients having moderate to severe asthma were evaluated for ABPA, of which 12 (37.5%) satisfied the revised ISHAM criteria for ABPA. Of the remaining 18 patients diagnosed as ABPA as per revised ISHAM criteria, 10 had COPD and 8 had bronchiectasis.
- All patients presented with increasing dyspnoea and dry cough (except productive in 2 patients only) and 11 with chest tightness or pain in addition to cough and dyspnoea suggesting an exacerbation of underlying lung condition. One patient had an unusual presentation of skin rashes and recurrent anaphylaxis.

Radiologic Findings

Chest Radiography

Chest radiographs showed heterogeneous and often non-specific findings including:

- Upper lobe fibrosis in 2 patients
- Bronchiectatic changes such as tram track lines and cystic changes in 8 patients
- Hyperinflated lung fields in 7 patients
- Patchy consolidation in 2 patients
- Bronchovascular prominence in 11 patients

HRCT Thorax revealed concomitant findings, with predominant features of

- Central bronchiectasis in 8 patients
- Mucous filled dilated bronchi with finger in glove appearance in 2 patients
- 2 patients had high attenuation mucus on HRCT, which is pathognomic for ABPA.
- Fibrobronchiectatic changes were seen in 2 patients
- 14 patients had mosaic attenuation with air trapping and emphysematous changes
- And 2 patients presented with lobar consolidation.

Immunologic Findings

Peripheral Eosinophilia

- All patients demonstrated peripheral blood eosinophilia of >500 cells/ µL (range 520–930 cells/µL).
- Mean absolute eosinophil count was 702 cells/µL

Total and Aspergillus fumigatus–Specific Serum IgE

- In all patients Total Sr. IgE was > 500 IU/ml (range 729 to 2759 IU/ml)
- Mean total IgE was 1492 IU/mL.
- Quantitative *A. fumigatus*–specific IgE levels were positive in all patients, exceeding the diagnostic threshold of 0.35 kUA/L

Skin Prick Test

- Immediate hypersensitivity to *A. fumigatus* was observed in 93.3% of cases.
- Mean wheal diameter: 6.8 mm.

4. Discussion

The fungal genus Aspergillus is an airborne filamentous saprophytic species that lives in soil and damp areas. A. fumigatus being a thermotolerant fungi i.e capable of surviving in environmental and elevated temperatures, is ubiquitous and its spores being 3–5 micron in size are readily inhaled and deposited in bronchioles.

Impaired clearance due to already abnormal airways in diseases like asthma, cystic fibrosis, COPD and bronchiectasis results in persistent colonization by Aspergillus species within these airways. However, a genetic predisposition seems to be required for progression to ABPA as suggested by studies showing familial occurrence of 4.9% [7]. HLA-DR molecules DR2, DR5, and possibly DR4 or DR7 contribute to susceptibility; whereas, HLA-DQ2 contributes to resistance, and a combination of these may determine the outcome of ABPA in CF and asthma.[8,9] A recent study demonstrated that a genetic variant in ZNF77 caused loss of integrity of bronchial epithelium[10], allowing Aspergillus conidia to germinate within the bronchial lumen, exposing their immunogenic components , resulting in Th2 type hypersensitivity response with release of Interleukins 4,5 and 13; leading to eosinophilic inflammation, raised total and A. fumigatus- specific immunoglobulin (Ig)E , mucus plugging and progressive bronchiectasis. Recent studies have identified that eosinophils exposed to A. fumigatus undergo a cytolytic cell death called EETosis, releasing chromatin fibres or eosinophilic extracellular traps (EETs)

(EETs) and cytotoxic granules into the airway lumen. The EETs provide an adhesive surface that traps A.fumigatus conidia and hyphae and are the primary component of the high- density mucus plugging seen in ABPA patients.[14]

Demographics and Predisposing Airway Disease:

- The mean age of patients diagnosed with ABPA in our study was (range 18 - 63 years) with no gender predominance.
- Though asthma and cystic fibrosis are the most common underlying chronic lung diseases associated with ABPA, in our study non cystic fibrosis Bronchiectasis and COPD were also equally important predisposing conditions and have been reported in other studies also.[11,12,13] ABPA is reported in about 10 % of asthma patients worldwide[1], but studies have shown a range between 7.4% to 60%.[15,16] The prevalence of ABPA was found to be 39% in a study of 57 patients with severe acute asthma admitted to an intensive care unit while it was 21% in the outpatient asthma group.[15] In our series; out of 32 asthmatic patients , 12 (37.5%) satisfied the revised ISHAM criteria for ABPA. 10 patients with COPD and 8 with non-cystic fibrosis Bronchiectasis were diagnosed as ABPA as per revised ISHAM criteria.
- Our study highlights the increasing recognition of ABPA beyond asthma and how any chronic lung disease with structural lung damage can predispose to fungal colonization and cause ABPA. Emerging studies suggest fungal sensitization worsens outcomes in COPD, supporting our findings

Tuberculosis Overlap in Indian Context

- In this study, of the 30 patients diagnosed with ABPA, 9 patients (30%) gave a history of being treated with anti-tuberculous drugs. These could be patients misdiagnosed as tuberculosis or it was a coexistence of tuberculosis (TB) which highlights a major diagnostic dilemma in TB-endemic countries.

- The clinical and radiological presentation of ABPA and TB have many similarities such as a presentation with cough, expectoration and dyspnoea and chest Xray showing upper lobe involvement, fibrosis, and cavitation; which contribute to diagnostic confusion.
- Agarwal et al. have also emphasized that ABPA is frequently misdiagnosed as smear-negative TB in India, leading to inappropriate anti-tubercular therapy and delayed treatment.

Immunological Markers

- Elevated IgE ($\geqslant$500 IU·mL^{-1}) and peripheral eosinophilia ($\geqslant$500 cells·μL^{-1}) were universal findings in this study. These markers reflect Th2-driven hypersensitivity and are central to diagnosis.
- Quantitative *A. fumigatus*–specific IgE levels were positive in all patients (100%), exceeding the diagnostic threshold of 0.35 kUA/L, which is an essential criteria required in the revised ISHAM guidelines.[2]
- Serum IgE levels in our cohort were comparable to international data, reinforcing the immunopathological consistency of ABPA across populations.
- Serial IgE monitoring is recommended for assessing treatment response and detecting relapses.

Radiological Significance

Central bronchiectasis remains the hallmark radiological feature of ABPA. HRCT plays a crucial role in:

- Early detection
- Disease classification (serologic ABPA-S vs ABPA-CB)
- Identifying irreversible fibrotic stage

Our findings emphasize that chest X-ray alone is insufficient and may delay diagnosis.

5. Clinical Implications

This study demonstrates:

- High burden of ABPA among asthma patients
- Significant emerging association with COPD and bronchiectasis
- Frequent overlap with post-tubercular lung disease
- Essential role of HRCT and immunological markers in diagnosis

Early identification in tertiary care settings is critical to prevent progression to irreversible fibrotic lung disease and respiratory failure.

6. Limitations

This was a single-centre study with a moderate sample size. Long-term outcomes and treatment response were not assessed. We propose to extend our study prospectively to all chronic lung diseases in the future. Multicentric studies will enhance our cohort and validate these findings.

7. Conclusions

ABPA is a substantial and under-recognized comorbidity among patients with chronic airway diseases, especially in India. Although frequently associated with asthma and cystic fibrosis, it is being increasingly recognized in COPD and non-cystic fibrosis bronchiectasis populations.

Universal positivity of *A. fumigatus*–specific IgE, along with elevated total IgE and peripheral blood eosinophilia confirms a robust antigen-driven disease process.

Pathognomic features in HRCT Thorax help in early detection of suspected ABPA patients.

ABPA is a highly treatable disease resulting in almost complete remission and improvement in quality of life if diagnosed and treated early. Hence it is important to have a high degree of suspicion of ABPA in patients with chronic lung disease and to apply clinical, laboratory and radiological criteria to diagnose ABPA as early as possible

Routine incorporation of specific IgE testing in high-risk chronic airway disease populations may enhance early diagnosis and prevent irreversible lung damage.

Systemic glucocorticoids and oral antifungal agents like itraconazole are the mainstay of treatment of acute ABPA along with environmental control measures preventing exposure to fungal allergens

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