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Serologic allergic bronchopulmonary aspergillosis (ABPA-S): Long-term outcomes

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Summary
Background and aim: ABPA is radiologically classified on the presence or absence of central bronchiectasis (CB) as ABPA-CB and serologic ABPA (ABPA-S) respectively. Few studies have described the follow-up of patients with ABPA-S. The aim of this retrospective study was to describe the outcomes of ABPA-S.
Methods: Patients were diagnosed as ABPA-S if they met all the following criteria: asthma, immediate cutaneous hyperreactivity to *Aspergillus fumigatus* antigen, total IgE levels >1000 IU/mL, *A. fumigatus* specific IgE levels >0.35 kUA/L and normal HRCT of the chest. They were treated with glucocorticoids and followed up with history, physical examination, chest radiograph and total IgE levels every 6 weeks to 3 months. In addition, an annual spirometry and a biennial HRCT chest were performed in all patients.
Results: Of the 55 patients with ABPA-S, 41 (17 men, 24 women; mean age, 38.3 years) consented for performance of repeat HRCT scans. The median duration of asthma prior to diagnosis of ABPA was six years. The duration of follow-up ranged from 24 to 77 months with the mean (SD) follow-up duration being 43.7 (10.1) months. There was improvement in FEV_1 but not the FVC values during the follow-up period (p values = 0.001 and 0.5 for FEV_1 and FVC respectively). There was no development of CB in any patient. Sixteen patients had a relapse during the follow-up period, and six patients were classified as glucocorticoid-dependent ABPA.
Conclusions: Although relapses are frequently seen, the long-term outcome of ABPA-S is good with no patient developing CB.

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Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a pulmonary disorder caused by complex immunological reactions to *Aspergillus fumigatus* that complicates the course of asthma and cystic fibrosis.[1,2] The prevalence of ABPA in asthma varies from 2 to 32% in special clinics,[3] whereas the prevalence in cystic fibrosis ranges from 2 to 15%.[4] The condition generally presents with poorly controlled asthma, hemoptysis, fever and weight loss.[5] The Rosenberg-Patterson criteria are most often used for diagnosis,[6,7] however there is no clear consensus on the number of criteria needed for diagnosis.[8] High-resolution computed tomography (HRCT) of the chest is the imaging modality of choice for the diagnosis of ABPA.[9] ABPA can be classified on HRCT chest as serologic ABPA (ABPA-S), ABPA with central bronchiectasis (ABPA-CB) and ABPA with central bronchiectasis and high-attenuation mucus (ABPA-CB-HAM).[10] While central bronchiectasis (CB) is considered to be a characteristic feature of ABPA, it is not essential for diagnosis, and CB is considered a late manifestation of the disease.[11]

Patients with ABPA who otherwise fulfill all diagnostic criteria but lack demonstrable abnormalities on CT chest are labeled as ABPA-S.[7,12–14] ABPA-S is generally believed to be the earliest stage of ABPA with lesser degree of immunological activity and a milder clinical course.[12] Long-term oral glucocorticoid therapy is often required to prevent progression of lung damage in ABPA.[15] Few studies have described the long-term outcomes of patients with ABPA-S.[7,12–14] Moreover, no study has performed HRCT chest during follow-up to document the development of CB in these patients. It is essential to monitor the radiological changes in this group of patients so as to determine the effectiveness of therapy or the need for additional therapy.

ABPA is a common problem encountered in our asthma clinic, and we have reported the clinical features and outcomes of more than 200 patients with ABPA.[10,16–19] In this study, using the same dataset we describe the long-term outcomes of patients with ABPA-S.

Material and methods

The current study is a retrospective analysis, and includes patients of ABPA-S diagnosed between January 2004 and December 2008 and followed till December 2010. The baseline characteristics of these patients have already been previously reported.[10,16–18] This study describes the follow-up of patients with ABPA-S. A written informed consent was taken from all patients and the study was approved by the Institute Ethics Committee.

We screen all patients of asthma in our Chest clinic with an *Aspergillus* skin test. Patients demonstrating immediate hypersensitivity in *Aspergillus* skin test are further investigated for ABPA with total and *A. fumigatus* specific IgE levels, *Aspergillus* precipitins, eosinophil count and HRCT of the chest. Patients are diagnosed as ABPA-S if they meet all the following criteria: (a) diagnosis of bronchial asthma (b) immediate cutaneous hyperreactivity to *A. fumigatus* antigen; (c) total IgE levels >1000 IU/mL; (d) *A. fumigatus* specific IgE levels >0.35 kUA/L; and, (e) normal HRCT of the chest **AND** any of the following criteria: (a) presence of serum precipitins against *A. fumigatus*; (b) fleeting opacities on the chest radiograph and, (c) total eosinophil count >1000 cells/μL.[19]

Aspergillus skin test

Was performed by injecting 0.2 mL of the *A. fumigatus* antigen (100 PNU/mL) intradermally in the forearm.[20] 0.2 mL of phosphate buffer saline is used as negative control. The injection site is examined every 15 min for 1 h, and then after six to 8 h. The reactions are classified as type I if wheal and erythema developed within a minute, reached a maximum after 10–20 min and resolved within 1–2 h. Type III reactions are defined by the presence of any amount of subcutaneous edema after 6 h.

Levels of serum IgE (total) and IgE (for *A. fumigatus*)

Were assayed with commercially available kits using the quantitative enzyme-linked immunosorbent assay (Demeditec diagnostics GmbH, Kiel, Germany) and the fluorescent enzyme immunoassay (UniCap Systems; Phadia, Stockholm, Sweden) as per the manufacturer's instructions.

High-resolution CT of the chest

Was performed on a 16-row, multiple detector, CT scanner (LightSpeed Plus; GE Medical Systems; Slough, UK) with a 512 matrix size. The scans were obtained with a scan time of 3 s in the supine position at full end-inspiration from lung apex to base. The image acquisition was contiguous and the images (1.25 mm at 10-mm intervals) were reconstructed using the high-spatial-frequency algorithm. The HRCT chest was reported by a radiologist (MG) as well as independently interpreted by a clinician (RA) unblinded to the patient identity or clinical presentation.

A. fumigatus precipitins

Were detected by the Ouchterlony's gel diffusion techniques according to the method of Longbottom and Pepys.[21]

Spirometry

Was performed using commercial dry rolling seal spirometer (Spiro RS-232; P.K. Morgan Limited; Kent, UK) and the forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC) measurements were recorded. Patients were classified as mild, moderate and severe obstruction as per the standardized practice in our laboratory.[22]

Total eosinophil count

Was performed by manually counting 100 cells on the peripheral blood film after determining the total white cell count on an automated blood cell analyzer.