A Contraversy to Traditional Manifestation of ABPA: ABPA Without Asthma


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SUMMARY
Allergic bronchopulmonary aspergillosis (ABPA) is a complex disease triggered by hypersensitivity reaction to allergens of Aspergillus species. Aspergillus fumigatus is the most common agent of the disease. ABPA is rarely presented in the absence of asthma, which is the principle criterion for its diagnosis. In this report, we present the case of a 43-year-old man without a history of bronchial asthma, who manifested with nonproductive persistent cough, bilateral nodular opacities and central bronchiectasis. Pathologic examinations of resected surgical specimens revealed features typical of ABPA. This is a rare case of ABPA in a non-asthmatic individual.

KEY WORDS: ABPA, asthma, Aspergillus fumigatus

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ÖZET
SIRADIŞI BİR ABPA OLGUSU: ASTIMSIZ ABPA

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INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) is a lung disease caused by hypersensitivity reactions to antigens of *Aspergillus* species, which is a genus of fungi with worldwide distribution (1).

Diagnostic criteria for ABPA include the presence of bronchial asthma, immediate skin test reactivity to *Aspergillus fumigatus*, elevated, total and *A. fumigatus*-specific IgE levels, pulmonary infiltrates (transient or fixed), central bronchiectasis, peripheral blood eosinophilia, and presence of precipitins against *Aspergillus* antigen (2).

However it is still quite challenging for the clinicians to achieve the diagnosis of ABPA because of different manifestations of the disease that makes fulfilling the diagnostic criteria impossible (3-5).

CASE

A 43-year-old male suffering from cough, dyspnea and hemoptysis was admitted to different medical center in December 2005. After detailed investigation (including sputum examination for acid fast bacilli, flexible bronchoscopy with mucosal biopsy, autoantibody detection), empiric antibiotic therapy had been given. Almost 2 years later, patient was admitted to our clinic for persistent non-productive cough. He was lifelong non-smoker and his past medical history was unremarkable.

Physical examination was normal on admission. Routine laboratory tests were in normal limits, except marked eosinophilia (1000/mm³, 10.4%). Chest X-ray showed bilateral non-homogenous nodular opacities (Figure 1). Thorax HRCT revealed a mass lesion in left hemithorax and multiple nodular opacities surrounding with parenchymal distortion and bronchiectatic areas in right hemithorax and left perihilar area (Figure 2). Thorax computerized tomography angiography excluded vascular origin. Due to non-diagnostic bronchoscopic mucosal biopsy, diagnostic thoracotomy was performed. Left upper lobe wedge biopsy revealed inflammatory cells in bronchial walls, peribronchial areas and parenchyma, bronchiectasis and mucus plugs containing eosinophils. Charcot-Leyden crystals and *Aspergillus* hyphaes were also seen (Figure 3).

Figure 1. Chest X-ray showed bilateral non-homogenous nodular opacities.

Figure 2. Thorax HRCT revealed a mass lesion on left hemithorax (A). Thorax HRCT showed bronchiectatic areas in right hemithorax and left perihilar area (B).
Based on histopathologic features detailed investigations for ABPA were performed. The serum total IgE level was > 5000 kU/L and specific IgE against \textit{A. fumigatus} was positive (class 5, 64.9 kU/L) by Pharmacia- UniCAP. Skin prick test was also positive to \textit{A. fumigatus} (Allergopharma, Reinbek-Germany). Pulmonary function test was normal and bronchial challenge test with methacholine via 5 breath method was negative.

The patient was accepted an ABPA despite lack of asthma as main criteria for the diagnosis according to Rosenberg-Patterson criteria. Antifungal (200 mg/day itraconazole) and systemic corticosteroid (0.5 mg/kg/day prednisolone equivalent deflazacort) was begun. Corticosteroid dosage was tapered with 6 weeks intervals. After 16 weeks, the serum total IgE level dropped to 800 kU/L and marked radiologic improvement on thorax HRCT was seen (Figure 4). So antifungal therapy was ceased. On the nineth month of the treatment, the serum total IgE and specific IgE against \textit{A. fumigatus} levels were dropped to 451 kU/L and 7.90 kU/L respectively. The patient was still on 6 mg/day deflazacort every other day. No asthmatic signs and symptoms were developed till now.

**DISCUSSION**

ABPA is a complex disease triggered by hypersensitivity reaction to allergens of \textit{Aspergillus} species, most commonly \textit{A. fumigatus}, which opportunistically colonize lungs of patients especially with asthma (6). As the symptoms and laboratory tests are not specific for ABPA, the diagnosis is very challenging and may be delay for years (7,8). A remarkable aspect was that in 13 patients of ABPA without asthma, an initial diagnosis of bronchogenic carcinoma was considered (9,10). Also in an analysis of 155 ABPA patients, Agarwal et al. determined that 65 patients had received antituberculous therapy in the past (2). Due to same reasons, the diagnosis had been also delayed almost 2 years in our patient.

Although Rosenberg-Patterson diagnostic criteria have been the most commonly used, today the diagnostic value of it is being criticized (1). In a study of 19 patients with ABPA made by Matsuse and his colleagues the positive factors of these criteria were indicated as asthma (84%), peripheral blood eosinophilia (100%), immediate skin reaction (82%), precipitating antibody against \textit{A. fumi-
gatus antigen (21%), increased serum total IgE (100%), pulmonary infiltration (85%), central bronchiectasis (70%). Similarly to our case, three of the patients (15%) did not have asthma as an initial symptom (7). Recently, Amitani et al. demonstrated experimentally that Aspergillus spp. produced substances which slowed ciliary beat frequency and damaged respiratory epithelium (11). This fact suggested that those substances could deteriorate mucociliary clearance and could lead to the process of the colonization of the airways. Bronchial asthma was suspected to be the accelerating factor in the development of ABPA, but not the premise or an essential factor (3).

ABPA was classified into five stages by Greenberger as acute stage, remission, exacerbation, corticosteroid dependent asthma and fibrotic end stage lung disease (12). Another classification made by Kumar suggests three stages according to the serologic and radiologic findings as ABPA-serology positive (ABPA-S), ABPA with central bronchiectasis (ABPA-CB) and ABPA with central bronchiectasis and other radiologic findings (ABPA-CB-ORF). According to the Kumar’s report, it is suggested that ABPA includes mild (ABPA-S), moderate (ABPA-CB) and severe (ABPA-CB-ORF) forms of disease (13). According to Greenberg, our patient is likely to be in acute stage, where as in severe (ABPA-CB-ORF) stage regarding to Kumar, why both antifungal and systemic corticosteroid therapy was given.

Glancy et al. reported 11 patients of ABPA without an evidence of asthma. But in those cases, some had developed bronchial asthma (14). Absence of asthma can be a good prognostic factor showing the early stages of the disease (13). From this point of view some authors advocates that asthma may not be initial criteria but may appear in the later stages of the disease (12). In nine month follow-up period, we observed no signs and symptoms of asthma. In addition, both radiologic and clinical improvements suggested that patient would have good prognosis. It is also recommended the life-long follow up in the ABPA-CB-ORF, so patient will be followed (13).

Itraconazole, an antifungal agent, appears to be an effective adjunctive therapy for ABPA. Treatment with itraconazole reduces bronchial inflammation and may prevent bronchial destruction and exacerbation in ABPA patients. On the other hand long-term prescription of an antifungal therapy may lead to resistance. The trials validating the use of itraconazole in ABPA patients with a dose of 200 mg/day, administered for a duration of 16 weeks as we did (15).

In conclusion, we suggest that the presence of asthma can indicate ABPA, but it is not essential. ABPA should be kept in mind in a patient with pulmonary nodules, peripheral blood eosinophilia and increased serum IgE level even if the absence of asthma.

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