

Development of Allergic Bronchopulmonary Aspergillosis with Central Bronchiectasis Over a 10-year Period: The Need to Recheck Allergen Sensitization

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Abstract

A 55-year-old woman visited our hospital for an investigation of central bronchiectasis, mucoid impaction and infiltrative shadows on chest CT. She had a 10-year history of bronchial asthma; however, her adherence to treatment was poor. Based on the presence of peripheral blood eosinophilia and immediate cutaneous reactivity to *Aspergillus fumigatus*, the patient was clinically diagnosed with allergic bronchopulmonary aspergillosis. Her condition and CT findings improved with systemic corticosteroid therapy. It was found that the patient had not been sensitized to *Aspergillus* 10 years earlier, indicating that single testing is inadequate for the early diagnosis of this disease.

Key words: allergic bronchopulmonary aspergillosis, *Aspergillus*, central bronchiectasis, early diagnosis, 10-year period

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Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is an immunological pulmonary disorder caused by hypersensitivity to *Aspergillus fumigatus* (*A. fumigatus*), that presents with asthma, recurrent pulmonary infiltrates and bronchiectasis (1). ABPA is a progressive disease, and a delay in diagnosis and treatment results in irreversible airway destruction leading to chronic respiratory infection or failure. The first step in the development of ABPA is the acquisition of *Aspergillus* hypersensitivity. In view of the importance of early diagnosis, criteria for the diagnosis of ABPA-seropositive and ABPA-central bronchiectasis have been proposed (2). The onset of ABPA typically occurs many years after the diagnosis of asthma is made (3). A long duration of asthma (median, 15; range, 1-48 years) prior to the diagnosis of ABPA was reported in a series of patients with ABPA (4); however, when the patients were sensitized is unknown. In a previous study, approximately 25% of subjects

with asthma were sensitized to *Aspergillus*, and a small fraction of them developed ABPA (3). Therefore, it is important to know whether a patient is sensitized to *Aspergillus*, although, if a patient is not sensitized at the initial diagnosis of asthma, it is unlikely that he or she will be followed up as a patient at risk for ABPA. In this communication, we describe the case of an asthmatic patient who was not sensitized to *Aspergillus* initially but developed ABPA with central bronchiectasis over a 10-year period, highlighting the need to recheck allergen sensitization.

Case Report

A 55-year-old woman visited our hospital for an investigation of abnormal shadows on a chest X-ray and CT. She had a 10-year history of bronchial asthma that had been diagnosed at a previous hospital. She was a nonsmoking office worker and had allergic rhinitis. She had no history of indoor or outdoor exposure to high levels of fungi. Previous laboratory data revealed a white blood cell (WBC) count of

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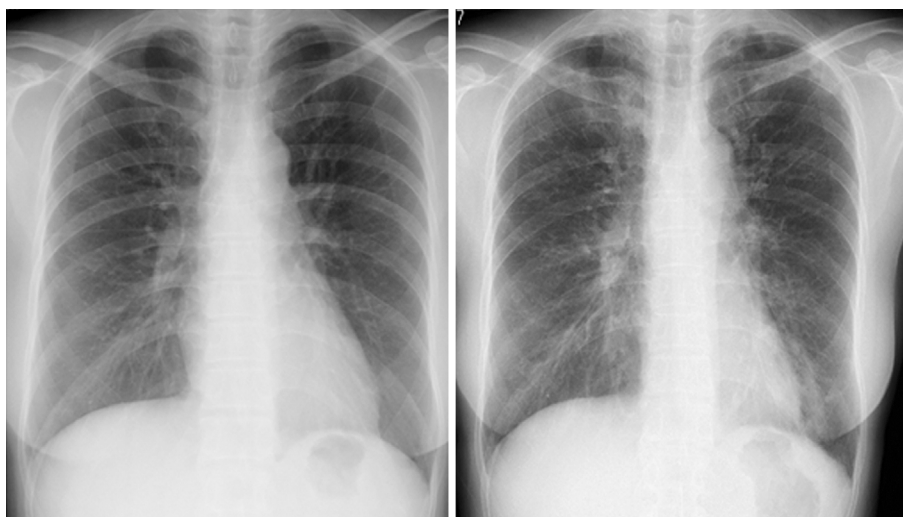


Figure 1. Chest X-ray films showing no abnormal findings (at 45 years of age, left panel) and bilateral infiltrative shadows (at 55 years of age, right panel).

6,500 cells/ μ L with 10% eosinophils and a total serum IgE level of 380 IU/mL. Specific IgE tests were positive for Japanese cedar, Japanese cypress, orchard grass and cats and negative for *A. fumigatus*, *Candida albicans*, *Alternaria alternata*, *Cladosporium herbarum* and *Penicillium notatum*. The sputum eosinophil count was 4%, the forced expiratory volume in one second (FEV1) was 2.17 L (88.9% of predicted) and the provocative concentration of methacholine causing a 20% fall in the FEV1 was 5,000 μ g/mL. A chest X-ray was normal at that time (Fig. 1). The patient was given budesonide at a dose of 400 μ g/day; however, her asthma was uncontrolled due to poor adherence to the treatment. Three years prior to the visit to our hospital, at 52 years of age, a salmeterol/fluticasone combination had been administered at a local clinic due to recurrent asthma attacks. In addition, since she complained of expectoration of purulent sputum, long-term macrolide therapy was added under a diagnosis of chronic respiratory infection. At 55 years of age, she was referred to our hospital with abnormal chest X-ray and CT findings on an annual medical examination. The chest X-ray and CT scan showed bilateral infiltrative shadows, central bronchiectasis and mucoid impaction (Fig. 1, 2). The laboratory data revealed a WBC count of 8,700 cells/ μ L with 15% eosinophils and a total IgE level of 431 IU/mL. Specific IgE to *A. fumigatus* was positive (1.28 UA/mL, class 2), and an immediate skin test for *A. fumigatus* yielded a positive reaction (flare, 35 $\times$ 35 mm; and wheal, 18 $\times$ 13 mm), whereas serum precipitins to *A. fumigatus* and both sputum and bronchoalveolar lavage fluid cultures were negative for bacteria and mycobacteria. Specific IgE antibodies to other fungi were negative. A pulmonary function test revealed an FEV1 of 1.30 L (57.3% of predicted), and the exhaled nitric oxide concentration was 59.9 ppb. We diagnosed the patient clinically with ABPA based of the criteria of Greenberger (positive for five of five minimal essential criteria for ABPA-central bronchiectasis) (2) rather than those of Rosenberg (positive for six of seven primary find-

ings and negative for secondary findings) (1) and initiated oral corticosteroid therapy (prednisolone: 20 mg/day; 0.5 mg/kg body weight). Two months later, the patient's condition and CT findings markedly improved (Fig. 3).

Discussion

In the *Aspergillus*-specific, IgE-mediated immune response, abnormalities of the airway and changes in mucus production and properties may contribute to the development of ABPA in patients with asthma (3). This disorder must be detected before bronchiectasis develops because the occurrence of bronchiectasis is associated with poorer outcomes, including progressive destruction of the lung parenchyma and loss of the lung function (3, 5). In Western countries, patients with cystic fibrosis are also at risk for developing ABPA since *A. fumigatus* frequently colonizes bronchiectatic or cystic airways and causes the disorder (3). In the present case, since the chest X-ray was normal at the time of diagnosis of asthma 10 years earlier, and the bacterial and mycobacterial cultures were negative, we speculate that there were initially no bronchiectatic airways similar to that observed in cystic fibrosis and that the central bronchiectasis was later caused by the development of ABPA. Since specific IgE antibodies to *A. fumigatus* were negative at the initial diagnosis of asthma, it is unknown when the patient became sensitized to *A. fumigatus* and developed ABPA. Her adherence to treatment was poor, and she did not receive regular checkups. Furthermore, she had few typical symptoms of ABPA, such as a low-grade fever, malaise and weight loss, and presented only with poorly controlled asthma and expectoration of purulent sputum. This may explain the delayed diagnosis of ABPA in the present case. A recent review of ABPA stated that because many patients with ABPA may be minimally symptomatic or asymptomatic, a high index of suspicion for ABPA should be maintained when treating any patient with bronchial asthma,

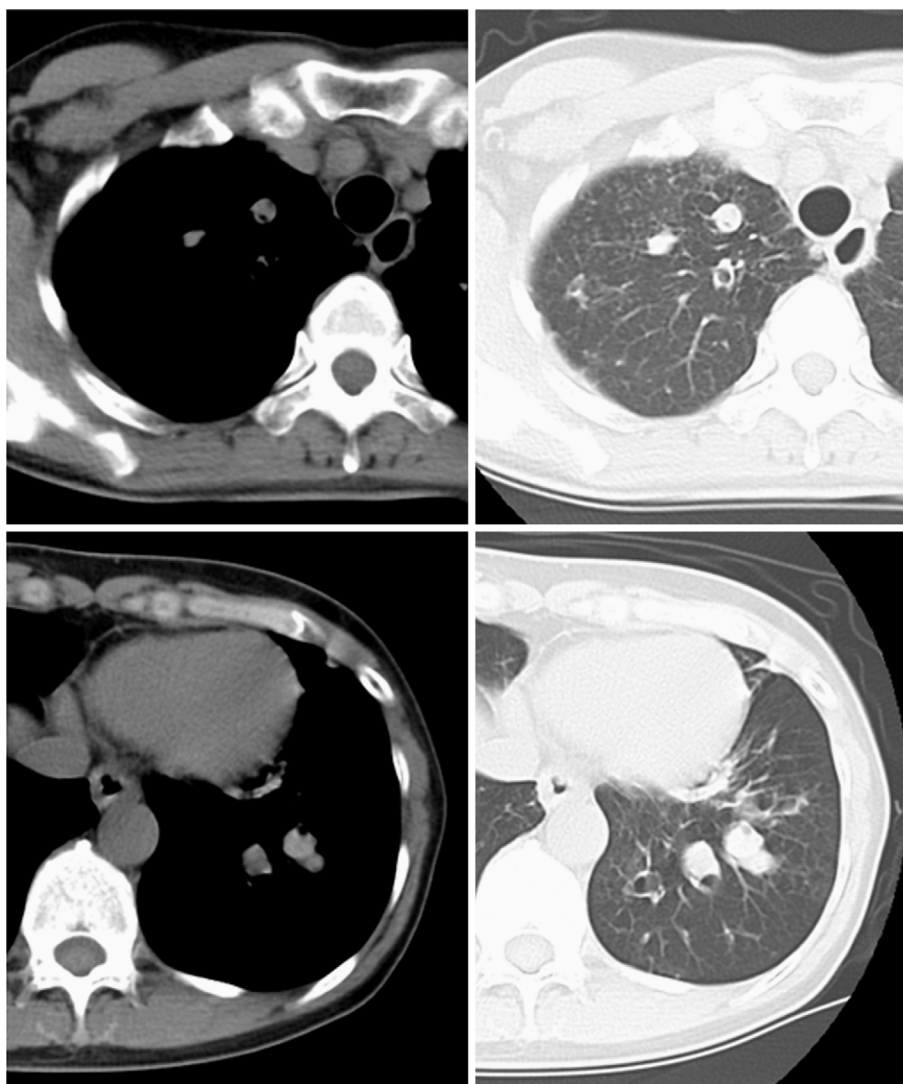


Figure 2. CT findings showing high-density nodules of mucoid impaction.



Figure 3. CT findings after 2-month treatment with an oral corticosteroid. After therapy, the mucoid impaction disappeared, while the central bronchiectasis remained.

whatever the disease severity or level of control (5). In addition, various genetic factors are involved in the pathogenesis

of ABPA (5); however, we did not investigate whether this patient was genetically predisposed. Developing a tool to

evaluate such genetic factors in real clinical settings is desirable. Since the current recommendation is to consider the use of an antifungal agent as a corticosteroid-sparing agent or as an alternative in case in which corticosteroids alone are ineffective (3, 5), we did not use antifungal agents, such as itraconazole, in this case. In conclusion, we would like to emphasize that single screening testing for sensitization to *A. fumigatus* is inadequate and that repeat tests should occasionally be considered. Furthermore, although *Aspergillus* is ubiquitous, identifying environmental sources that show particularly high levels of *Aspergillus* or support the active growth of *Aspergillus* is advised (3).

The authors state that they have no Conflict of Interest (COI).

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