Recurrence of Allergic Bronchopulmonary Aspergillosis in the Posttransplant Lungs of a Cystic Fibrosis Patient*

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Cystic fibrosis (CF) is an autosomal recessive disease of exocrine origin. Allergic bronchopulmonary aspergillosis (ABPA) is an immunologic disorder caused by colonization of the airways with Aspergillus fumigatus. A fumigatus has been cultured from posttransplant lungs in CF patients. Colonization of posttransplant lung with Aspergillus is a recognized phenomenon. In this case report, however, we present a patient who developed ABPA both before and after lung transplant. This patient meets the criteria for ABPA based on serologic results. ABPA may be a complication in post-CF lung transplant patients and serologic analysis should be considered when eosinophilia and pulmonary infiltrates or decline in lung function occurs.

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Key words: allergic bronchopulmonary aspergillosis; cystic fibrosis; lung transplant

Abbreviations: ABPA = allergic bronchopulmonary aspergillosis; CB = central bronchiectasis; CF = cystic fibrosis

Allergic bronchopulmonary aspergillosis (ABPA) is a pulmonary disease that results from an immunologic response to Aspergillus fumigatus. Reports in England relating pulmonary infestation with Aspergillus to hypersensitivity appeared in the literature as early as 1951.1 The first cases of ABPA discovered in the United States were documented more than 25 years ago.2,3 Nonspecific findings such as wheezing, eosinophilia, and pulmonary infiltrates on chest radiograph, as well as its indolent nature, make ABPA difficult to diagnose. ABPA may be completely asymptomatic, adding to diagnostic difficulty.4

Five criteria were considered important for diagnosis: (1) asthma; (2) central bronchiectasis (CB); (3) elevated total IgE level (>1,000 ng/mL); (4) immediate cutaneous reactivity to A fumigatus; and (5) elevated serum IgE or IgG antibodies to A fumigatus.4 Treatment of patients with ABPA is facilitated by staging their disease. This disease may progress through five stages: acute, remission, recurrent exacerbation, corticosteroid-dependent asthma, and fibrotic end-stage lung disease.5 All but the last two stages may enter remission. The fibrotic stage is irreversible. A patient with ABPA may have no CB and few of the criteria for ABPA except asthma and positive skin tests for A fumigatus and positive serologic test results. This condition is labeled ABPA serologic.6 To reverse the acute or exacerbation stage, the basis of treatment is oral steroids.

Cystic fibrosis (CF) is an autosomal recessive exocrine disease with pathologic changes affecting the tracheobronchial tree, the pancreas, and the GI tract. Abnormalities in the sweat glands lead to diagnostic findings of elevated chloride levels in sweat. CF is the most common lethal genetic disease of whites in the United States. Pulmonary manifestations of this disease are the major cause of morbidity and mortality. Infections with mucoid-producing Pseudomonas aeruginosa, in particular, lead to pulmonary complications.7

The association between CF and ABPA was first made in 1967.8 A fumigatus has been found in the sputum in as many as 57% of CF patients.9 As in ABPA, chest radiographic findings such as pulmonary infiltrates and CB are a feature of CF.10 Since patients with CF but free of ABPA may show eosinophilia, precipitins (30%), and skin reactivity to A fumigatus (60%),11 appropriate serologic studies are important for the diagnosis of ABPA.12

CASE REPORT

A 29-year-old white man was diagnosed as having CF at birth. He was symptom free until 4 years of age, at which time he began to have episodes of wheezing. At 6 years of age, he was hospitalized with wheezes thought to be associated with CF. He was hospitalized next in July 1979 at the age of 12 years with similar symptoms. He was diagnosed as having ABPA in 1980 when he presented with severe bronchospastic episodes. At this time, his serum total IgE level was 72,381 ng/mL with an anti-Aspergillus IgE index of 4.1 and an IgG index of 2.8 (Table 1). Serologic evaluation also showed a positive precipitin reaction against A fumigatus. The respiratory symptoms responded poorly to therapy until corticosteroids were used. Then the initial as well as subsequent episodes were controlled with prednisone until 1984.

On October 17, 1984, his serum IgE level was 3,500 ng/mL and he was asymptomatic. At this time, he was put on a 3-month

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*(Af=A fumigatus.)
course of alternate-day prednisone and eventually his condition came under control. In 1994, he was sent to the University of North Carolina for evaluation for lung transplant. On August 16, 1994, his FEV\textsubscript{1} was 0.72 L, which was 22% of predicted, and he clearly had terminal respiratory disease. His condition deteriorated, culminating in a hospitalization 4 months later in December 1994 for progressive respiratory failure.

On December 7, 1994, he received two lower lobe lung transplants, one from each of his brothers. Neither brother had a history suggestive of asthma or ABPA. All lung tissue was removed from the recipient.

He did well until April 16, 1995, at which time he was hospitalized for a combination of pulmonary edema evident on chest radiograph and hypoxemia. Cytomegalovirus and acute rejection (biopsy specimen proved) were thought to be the source of these problems. After successful treatment, he did well until January 11, 1996, at which time he underwent a routine 1-year surveillance bronchoscopy and transbronchial biopsies. Biopsy results showed an eosinophilic infiltrate, but no evidence of cytomegalovirus or rejection. Fungal cultures were negative. The FEV\textsubscript{1} of 2.68 L and a FVC of 2.95 L were 75% of predicted for both. For presumed rejection, he was treated with prednisone, 40 mg for 3 days with a subsequent prednisone dosage reduction. The steroid intervention was successful. However, on March 20, an abrupt fall in spirometry associated with complaints of wheezing and shortness of breath were noted. FEV\textsubscript{1} fell from 3.0 to 1.65 L, and FVC dropped from 4.0 to 2.7 L. This decrease in lung function appeared to be associated with physical activities in his attic. He was treated successfully with IV methylprednisolone sodium succinate (Solu-Medrol) followed by a prednisone dosage taper.

By April 1, his pulmonary function test results were back to baseline. After lung transplant, the patient’s total IgE and IgG index were low, but IgE index and precipitins against \textit{A fumigatus} were positive. Serologic analyses of a sample from April 19, 1996 were all positive, clearly consistent with a diagnosis of ABPA (Table 1).

**DISCUSSION**

ABPA and CF may present with similar clinical findings. Chloride sweat test and serologic analysis for ABPA make diagnosis of both diseases possible. These diseases are not mutually exclusive, as ABPA may occur in patients with CF. Presented in this study is a case of an individual who initially presented with CF, was diagnosed with ABPA, and underwent a bilateral lung transplant. The bronchiectatic airways of CF patients are suitable for colonization by \textit{A fumigatus}. Aspergillus has been cultured from the sputum of posttransplant CF patients.13 In addition, cases have been reported of patients fulfilling criteria for ABPA after lung transplant.14 This is interesting in light of the fact that neither the donor nor the recipient were initially diagnosed as having ABPA. Our patient, however, is the first case to our knowledge of a patient presenting with ABPA before living donor transplantation, then developing ABPA again posttransplant. This case represents a recurrence of ABPA in a postlung transplant patient who required therapeutic intervention with prednisone. The fact that he had ABPA pretransplant and that the lungs came from related family members brings up an interesting question of genetic predisposition. The issue of immune suppression posttransplant is also pertinent. It remains to be seen if the progress of ABPA posttransplant will reflect the pretransplant course, and what role CF will have in its presentation.

Finally, in recipients of lung transplants, the role of the lung as an immunologic organ must be considered in future cases. Although information on immune responses of human lungs is limited, long-term antibody production in canine lung allografts has been demonstrated to persist as long as 320 days.15 This persisting antibody production may have implications both for protection of the lung graft recipient or for induction of pulmonary disease.

**REFERENCES**

1 Hinson KFW, Moon AJ. Bronchopulmonary aspergillosis. Thorax 1951; 7:317-33