Allergic bronchopulmonary aspergillosis (ABPA) can cause severe worsening of the respiratory condition in patients with cystic fibrosis. Treatment can result in steroid dependency and serious adverse events. A dramatic and rapid improvement of respiratory symptoms and lung function after a single dose of anti-IgE antibody (omalizumab) in a 12-year-old girl with cystic fibrosis and ABPA is described. This is the first report of this experimental treatment. It suggests an important role for IgE in the pathogenesis of ABPA and offers new therapeutic possibilities.

**Case History**

A 12-year-old girl had been diagnosed with cystic fibrosis directly after birth because of meconium ileum (genotype dF508/dF508). From infancy she had mild to moderate lung problems requiring antibiotic treatment three to five times a year. From age 5 years she was colonised with *Pseudomonas aeruginosa* and *A fumigatus*. At age 8 years she had more severe signs of cough and exercise-induced asthma. She developed pulmonary infiltrates and bronchiectasis and signs of severe airflow obstruction (forced expiratory volume in 1 s (FEV₁) fell from 105% to 34% of predicted). Blood testing revealed eosinophilia, marked increase in total serum IgE level (5200 IU/ml), positive *Aspergillus*-specific IgE-radio allergosorbent test (class 4–5) and positive precipitating IgG antibodies to *A fumigatus*. Treatment for ABPA involves attenuation of the inflammatory and immunological activity with corticosteroids and reduction of the antigen burden from fungal colonisation with antifungal agents. Long-term treatment is often required because of exacerbations that repeatedly occur when corticosteroid treatment has been tapered. Serious adverse events to corticosteroids are frequent in these patients. In this report, we successfully treated a patient with recombinant anti-IgE antibody (omalizumab).

**Discussion**

To our knowledge, this is the first patient with cystic fibrosis with ABPA to be treated with omalizumab. There was a repeated improvement in symptoms and normalisation of lung function within 2–4 h of administration of the drug. Several lessons can be drawn from this observation.

Omalizumab improves asthma control in patients with severe allergic asthma, reducing inhaled corticosteroid requirements. Although in patients with asthma the exacerbation rate declines during treatment, the effects on lung function remain relatively small. The dramatic improvement in both respiratory symptoms and FEV₁ in our patient suggests that omalizumab might offer a new therapeutic approach to patients with ABPA. Of course, our unblinded observations are not ultimate proof of the efficacy of omalizumab in ABPA. However, the striking, consistent and repeatable effects of subsequent administrations...
Anti-IgE in ABPA

The pathogenesis of ABPA remains complex and confusing. In all patients, very high total serum IgE levels and high levels of IgE anti-Aspergillus antibodies are seen. There seem to be quantitative and perhaps qualitative differences in the B cell IgE antibody responses between those with ABPA and those without ABPA.1 In ABPA, there are also increased amounts of IgG and IgA anti-Aspergillus antibodies, which reflect the balance between T helper cells types 2 and 1 in the response to Aspergillus antigens in these patients.2 To date, it has not been clear whether extreme amounts of IgE play a role in the pathogenesis of ABPA or whether it is only an epiphenomenon. The timing of the effects after administration of omalizumab in our patient suggests that IgE antibody might have an important role in the signs of airflow obstruction in ABPA. The serum levels of free IgE are reduced in a dose-dependent manner within 2 h of subcutaneous administration of omalizumab. The half-life of the drug in serum is about 22 days.3 In our patient, clinical improvement was observed within several hours, lasting for 2–3 weeks.

The diagnosis of ABPA in cystic fibrosis is difficult because many of the diagnostic criteria overlap with common manifestations of cystic fibrosis. The diagnosis is based on the presence of five or more essential criteria as proposed by the international consensus committees,1 and specific tests are lacking. When our observation is confirmed in other patients, the rapid and clear improvement of clinical signs and lung function after a single dose of omalizumab might be used as a helpful diagnostic test for ABPA.

LUNG ALERT

Inducible bronchus-associated lymphoid tissue and the pathogenesis of rheumatoid lung

Bronchus-associated lymphoid tissue (BALT) comprises submucosal lymphoid cells analogous to Peyer’s patches but located in association with large airways. It is generally not found in normal mouse or human lung tissue. Pulmonary infection or inflammation in mice leads to the development of lymphoid follicles that are not restricted to the upper airways, termed inducible BALT (iBALT). In this study the authors examined lung biopsies from patients with a variety of interstitial diseases including idiopathic pulmonary fibrosis, hypersensitivity pneumonitis and lung disease in association with rheumatoid arthritis (RA) and Sjogren’s syndrome (SS). Although small amounts of lymphoid aggregates were found in the non-autoimmune conditions, samples from the patients with RA and SS had more and larger lymphoid areas. The authors then proceeded to investigate the potential roles and causes of this well-organised iBALT. First, venules and lymphatic vessels were consistently found within the follicles and it was felt they were likely to facilitate entry and exit of immune cells. Second, levels of certain cytokines involved in lymphoid organogenesis and T helper type 2-driven pathology, as well as levels of the autoantibody anti-cyclic citrullinated peptide (anti-CCP) in BAL fluid, correlated well with the amount of iBALT. Third, dense areas of collagen deposition and myofibroblast activity around the follicles were seen in the patients with highly organised iBALT.

These findings suggest that iBALT may have a significant role in the pathogenesis of interstitial lung disease seen in association with connective tissue disorders. Further understanding of the mechanisms involved could be used to develop novel treatments.

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