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Anti IgE antibody as treatment of allergic bronchopulmonary aspergillosis in a patient with cystic fibrosis

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Abstract. – Allergic bronchopulmonary aspergillosis (ABPA) occurs in 7-9% of patients with cystic fibrosis (CF) and causes a worsening of lung function and respiratory symptoms. Standard treatment of ABPA consists of oral steroids; however, higher corticosteroid therapy associated to antifungal agent (itraconazole) long-term treatments are often required to reduce respiratory exacerbations and to prevent progressive lung damage. Here we describe the case of a girl with CF who experienced clinical and functional improvement over 12-months treatment with omalizumab. At birth, our patient was diagnosed with mild-to-moderate CF and from childhood she underwent annual cycles of antibiotic and corticosteroid therapies. At 12 years, she presented with a worsening respiratory condition, asthma symptoms and reduced lung function (FEV_1 of 78%). Blood tests showed an increased concentration of plasma total IgE and positive specific IgE antibodies to Aspergillus fumigatus; allergic skin tests were also positive for A. fumigatus. The patient started steroid therapy but had impaired glucose tolerance due to long-term steroid use. Subcutaneous omalizumab 300 mg every two weeks was initiated and after 14 weeks she had improved respiratory symptoms (FEV_1 99%) and a marked reduction in the use of systemic antibiotic and corticosteroid therapies. No side effects were reported. Our case shows that therapy with omalizumab for a prolonged period can resolve symptoms of asthma.

Key Words:
Anti IgE antibody, Bronchopulmonary aspergillosis, Cystic fibrosis, Omalizumab.

Introduction

In 2010, Brinkman et al[1] reported worsening of lung function with steroid dependency in a patients with allergic bronchopulmonary aspergillosis (ABPA), despite initial improvement with long-term anti-IgE therapy omalizumab.

ABPA occurs in 7-9% of patients with cystic fibrosis (CF)[2] and often manifests as wheezing, increased cough, shortness of breath, pulmonary infiltrates and bronchiectasis. ABPA causes a worsening of lung function and respiratory symptoms in patients with CF. Standard treatment consists of oral steroids and, for refractory cases, oral antifungals may be required[3].

Long-term treatment with oral steroid is often required to reduce exacerbations that occur when steroid therapy is stopped[4]. Frequently, patients with ABPA develop serious adverse events to corticosteroids[4].

Case Report

We describe the case of a girl who experienced significant clinical and functional improvement during a 12-month treatment course with omalizumab. The 13-year-old girl was diagnosed with CF at birth (DF508-W1282X). From childhood, she showed mild-to-moderate symptoms and underwent annual cycles of antibiotic therapy. At the age of 12 years, she presented with a worsening respiratory condition, development of asthma symptoms and decline in lung function from an FEV_1 of 97% to 78%. Blood tests showed an increased concentration of plasma total immunoglobulin E (IgE; 695 IU/mL) and positive specific IgE antibodies to *Aspergillus fumigatus* (5.45 IU/mL); moreover, allergic skin tests were positive for *A. fumigatus*. After APBA diagnosis, the patient started steroid therapy, but to resolve impaired glucose tolerance due to long-term steroid use, we considered an alternative treatment. Omalizumab was introduced at a single subcutaneous dose of 300 mg every two weeks, calculated on the weight and total IgE concentration. After 14 weeks from the beginning of omalizumab therapy, the patient showed an improvement in respiratory symptoms with a FEV_1 of 99% (Figure 1), a marked reduction in the use of systemic antibiotic

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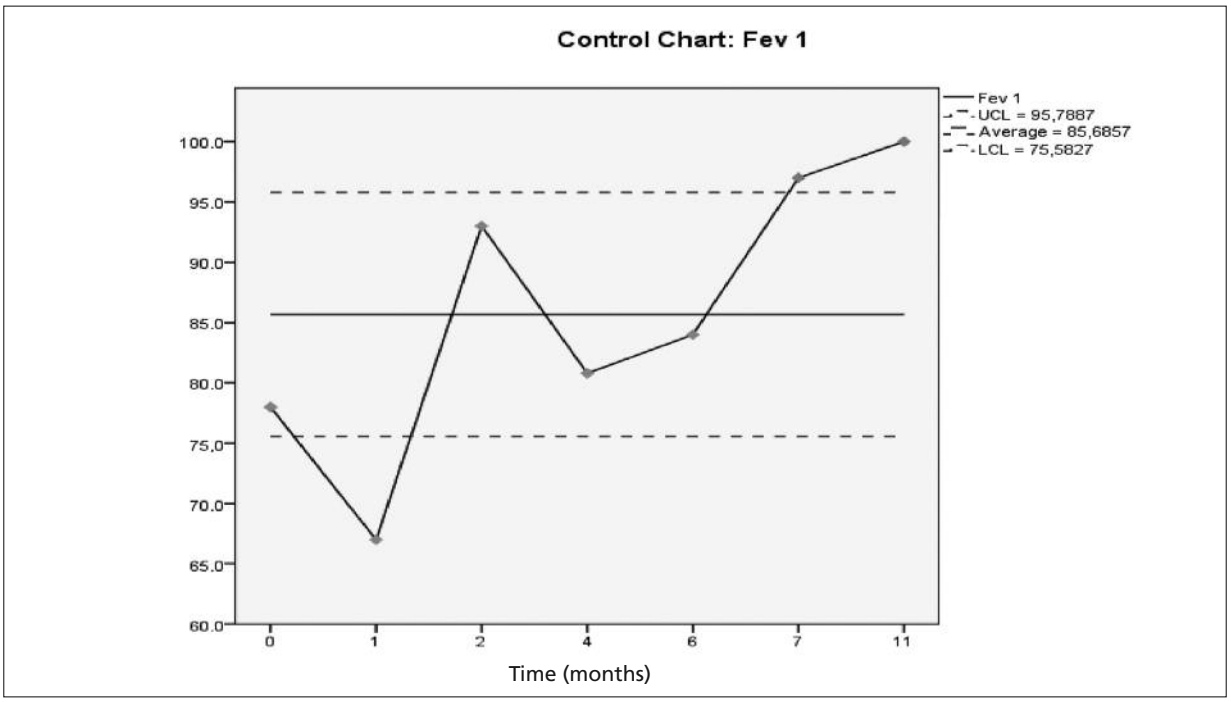

Figure 1. FEV_1 values increase from the baseline visit to the last visit (11 months later). At the fifth and at the sixth visit (7 and 11 months later the baseline visit) FEV_1 values are 1 sigma (standard deviation of the mean) distant from the FEV_1 mean value.

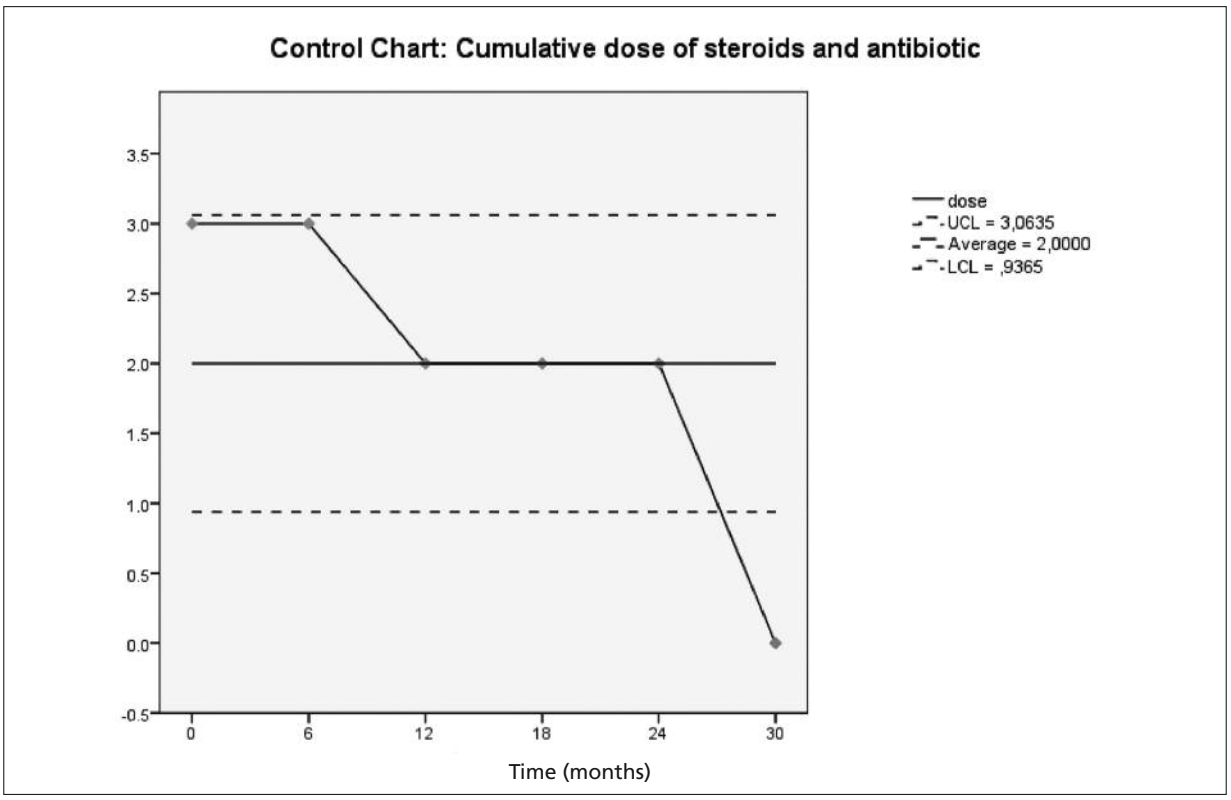

Figure 2. The cumulative dose of steroids and antibiotics taken by the girl has steadily declined in the weeks. After 30 weeks of treatment the dose is 2 sigma distant from the mean value.

and corticosteroid therapies (Figure 2), and experienced no side effects. In the previous year, she received antibiotic and corticosteroid therapy almost once a month. From 14 to 26 weeks, she received once antibiotic and two steroid treatments; from 22 weeks, neither were necessary.

Discussion

As reported in previous articles, there are other cases of patients with CF who have had improved clinical symptoms and spirometric values after therapy with anti-IgE. The first of these by van der Ent et al[5] describes a young girl with CF that improved after one single dose of omalizumab. Kanu et al[6] reported a case of CF and ABPA treated at third exacerbation with omalizumab with improvement. Lebeque et al[7] described two cases of adolescents with CF, in which ABPA exacerbations were treated by anti-IgE therapy (omalizumab) and both showed rapid improvement after 3 and 2 weeks, respectively. Similar findings were observed in two patients described by Zirbes et al[4], who both presented with particularly high IgE levels that required high doses of omalizumab. The elevated doses of omalizumab in these cases seemed to contribute to the greater degree of improvement seen.

However, our case shows that therapy with omalizumab for a prolonged period (12 months in this case) can resolve symptoms of asthma by reducing wheezing and dyspnoea with normalization of spirometric values.

These cases demonstrate the important role of the IgE in the pathogenesis of ABPA and suggest that omalizumab can provide a valid alternative treatment in patients with CF, one that can reduce the use of steroid therapy and was shown to be effective not only in the short-term but also over a prolonged period up to 1 year. Our findings in this case add to the accumulating anecdotal evidence demonstrating the safety and efficacy of omalizumab in patients with CF and ABPA.

Statement of Interest

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Conflict of Interest

The Authors declare no conflict of interest.

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