Effective Anti-immunoglobulin-E Antibody Treatment of a Patient With Allergic Bronchopulmonary Aspergillosis

Tratamiento efectivo con anticuerpo antiinmunoglobulina E en un paciente con aspergilosis broncopulmonar alérgica

To the Editor:

Allergic bronchopulmonary aspergillosis (ABPA) develops as the result of a hypersensitivity reaction to the *Aspergillus* fungus and is associated with a form of asthma that is difficult to manage. Some studies indicate that inhaled corticosteroids achieve a good level of control in a substantial proportion of patients, with oral corticosteroids reserved for patients who fail to respond to the inhaled form.[1] When treatment with oral corticosteroids has proven ineffective, the use of antifungal azoles has occasionally been successful.[2] A recently reported case indicated that treatment with anti-immunoglobulin-E antibodies (omalizumab) could be effective when standard treatments failed.[3] We describe the case of a man with life-threatening, difficult-to-control asthma due to ABPA who experienced significant clinical and functional improvement in response to treatment with omalizumab.

A 71-year-old man (a non-smoker) was diagnosed with asthma at the age of 50 years. He was initially treated with inhaled budesonide, salmeterol and terbutaline. This treatment regimen maintained forced expiratory volume in 1 second (FEV_1) at normal levels, and treatment with oral corticosteroids was only necessary on a handful of occasions. When the patient was 62 years old, a decline in FEV_1 to 58% of predicted was observed, although with no worsening of symptoms or increase in exacerbations. The option of prescribing oral corticosteroids was ruled out in favor of increasing the inhaled corticosteroid dose. From the age of 65 years, the patient experienced progressively worsening symptoms, with several exacerbations yearly (more than 3) that required admission to hospital, and, on 1 occasion, orotracheal intubation. By this time, FEV_1 had declined to around 36% of predicted. When the patient was 68 years old, he was diagnosed with ABPA on the basis of the following findings: asthma, increased serum immunoglobulin-E levels (327 U/L), raised eosinophil count in blood (2200/μL), a skin prick test that was immediately positive for *Aspergillus* species, and proximal bronchiectasis as evidenced by a high-resolution computed tomography scan. Given the difficulty in controlling the patient's asthma (values of between 8 and 10 in the asthma control test of Vega et al[4]) and the need for high doses of corticosteroids (deflazacort, 30 mg/d), it was decided to treat him with 225 mg of omalizumab every fortnight. The symptoms were brought under control (with asthma control test scores consistently over 20), and the patient improved to the extent that, after the second dose of omalizumab, he only presented dyspnea in response to strenuous effort. In the 20 months in which the patient took omalizumab, he experienced only 1 exacerbation—6 months after commencing the treatment—that did not require admission to hospital; furthermore, symptoms continued to improve and FEV_1 rose to 53% of predicted. By the end of the third month it was possible to discontinue treatment with deflazacort.

The pathogenesis of ABPA, which is an exaggerated reaction to *Aspergillus* antigens, is complex and has not yet been fully clarified. Nonetheless, the increase in immunoglobulin-E levels observed in these patients makes treatment with omalizumab a reasonable option a priori. In the literature we were only able to locate 1 similar case report, about a patient with cystic fibrosis and ABPA who showed clinical and functional improvement following administration of omalizumab.[3]

Our patient was experiencing progressive lung function loss, accompanied at a later stage by difficult-to-control symptoms and frequent admissions for severe asthma exacerbation. With a view to determining whether there was any concurrent process that might explain the progressive course of disease in this patient, we conducted a study that resulted in a diagnosis of ABPA on the basis of compliance with the 5 main ABPA criteria established by Rosenberg et al.[5] Despite high doses of inhaled corticosteroids and verification of correct inhalation technique, no appreciable improvement was achieved. A switch to treatment with oral deflazacort also failed to produce a positive outcome. With few other therapeutic options available, we prescribed omalizumab on the basis that it might possibly benefit our patient. Clinical response by the end of the first 2 months of treatment was very satisfactory, as reflected in asthma control test scores of over 20. After 20 months, FEV_1 had climbed from 36% to 53% of predicted–even though significant improvement in lung function occurs infrequently in patients treated with omalizumab according to a recent review.[6] Our patient also had only 1 subsequent exacerbation, 6 months after commencing treatment with omalizumab; since this exacerbation responded to treatment with oral corticosteroids, hospitalization was not necessary. Treatment with deflazacort was discontinued after 4 months.

In sum, omalizumab may prove to be an effective treatment option for patients with ABPA and asthma that is refractory to treatment with inhaled and oral corticosteroids. It would be interesting to test omalizumab for this particular indication in an ad-hoc clinical trial.

References

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