

Conflict of interest

The author states that there was no conflict of interest at the time the manuscript was written.

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Álvaro Peña-Irún

Centro de Salud El Sardinero, Santander, Cantabria, Spain

E-mail address: alvaro290475@hotmail.com

Role of omalizumab in the management of allergic bronchopulmonary aspergillosis in patients with cystic fibrosis[☆]



Papel de omalizumab en el tratamiento de la aspergilosis broncopulmonar alérgica en pacientes con fibrosis quística

Dear Editor,

Allergic bronchopulmonary aspergillosis (ABPA) is a cystic fibrosis (CF) disorder associated with accelerated pulmonary compromise.^{1–3} The treatment focuses on controlling inflammation and preventing the progression of lung injury.^{2,4} Systemic glucocorticoids constitute the basis of treatment^{1,4–7} for exacerbations and maintenance treatment to prevent progressive lung injury; they are usually administered in combination with an antifungal, such as itraconazole, in order to reduce the fungal antigen load.^{1,3,7,8} Side effects caused by corticosteroids have made it imperative to search for therapeutic alternatives,^{1,7} and omalizumab stands out among them. We present 3 cases of ABPA in CF patients treated with said drug.

First case: A 14-year-old male patient was diagnosed with ABPA. Pulmonary function at the time of diagnosis: forced expiratory volume (FEV)₁ 1.84 l (59%); forced vital capacity (FVC) 2.23 l (59.8%). Total IgE was 4177 kU/L. CT scan of the lungs (Fig. 1A) showed bilateral pseudonodules and aspergilloma in the right upper lobe. Treatment was started with prednisone 60 mg/day and itraconazole, which had to be replaced with voriconazole (200 mg/12 h) due to digestive intolerance. Having achieved clinical and spirometrical

improvement, corticosteroids were reduced; however, symptoms and spirometry results worsened, so glucocorticoids were once again increased and omalizumab was added (450 mg/15 days). Seven months after starting with omalizumab, pulmonary function remained stable (FEV₁ 2.90 l [82%], FVC 4.23 l [99.3%]), and both glucocorticoids and voriconazole were suspended.

Second case: A 29-year-old female patient diagnosed with a fourth re-exacerbation of ABPA. Pulmonary function at the time of diagnosis: FEV₁ 1.2 l (36.4%); FVC 2.03 l (55.3%). Total IgE was 1057 kU/L. CT scan of the lungs (Fig. 1B) showed cystic and central saccular bronchiectasis as well as lingular atelectasis. Treatment with prednisone (40 mg/day) and itraconazole (200 mg/12 h) was resumed. Since the patient suffered multiple re-exacerbations and frequently needed systemic glucocorticoids, she started receiving omalizumab (300 mg/month). Eighteen months after starting omalizumab, her pulmonary function remained stable (FEV₁ 1.45 l [45%], FVC 2.25 l [62%]) and improvements were observed on radiography. Glucocorticoids have been suspended, and she has not suffered new episodes of ABPA.

Third case: A 26-year-old female patient diagnosed with a second episode of ABPA in one year. Pulmonary function at the time of diagnosis: FEV₁ 1.9 l (62%); FVC 3.8 l (109%). Total IgE was 1213 kU/L. CT scan of the lungs showed bilateral nodular masses and central bronchiectasis (Fig. 1C). The treatment was resumed with 40 mg/day of prednisone and 200 mg/12 h of itraconazole. A month later, and having improved in terms of her clinical condition and blood test levels, the corticosteroid dose was reduced, resulting in pulmonary function compromise. Given this situation and the fact that the patient had 2 episodes of ABPA in one year, we decided to

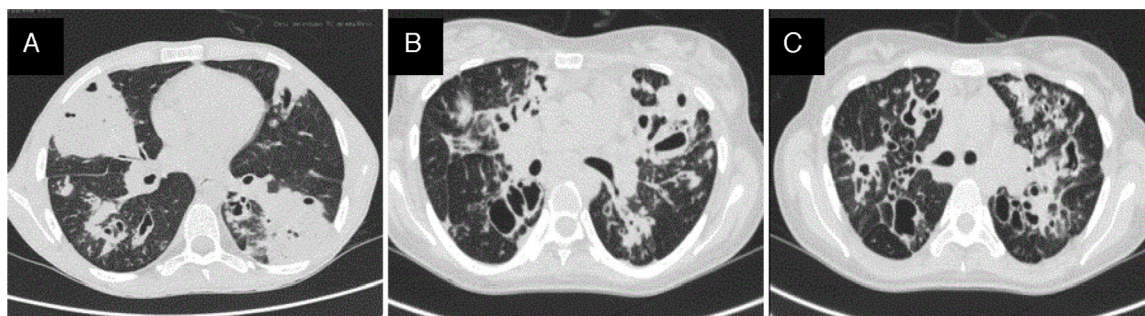


Fig. 1. Computed tomography of the lungs. (A) Bilateral pseudonodules. (B) Cystic and central saccular bronchiectasis. (C) Bilateral nodular images and central bronchiectasis.

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initiate treatment with omalizumab (600 mg every 15 days). Having achieved clinical and spirometrical stability, glucocorticoids were progressively withdrawn until they were fully suspended, along with itraconazole. At present, 5 months after starting omalizumab, the patient remains clinically stable with FEV₁ 2.25 l (74%) and FVC 4.03 l (116%).

Omalizumab, a monoclonal antibody anti-IgE,^{1,2} has been used sporadically to treat patients with ABPA and CF in an attempt to decrease or substitute glucocorticoids.^{1,3–7} It is generally used in patients with recurrent exacerbations and frequent hospitalisations, who need to take glucocorticoids on a long-term basis,¹ are dependant on⁶ or resistant to corticosteroids, or experience many side effects.^{1,2,5,9} In order to assess the therapeutic response to omalizumab, the recommendation is to quantify the levels of free IgE,^{2,6} its decrease being correlated with clinical improvement.² Total IgE is not useful to monitor treatment,⁵ as it increases 2 to 5 times during the course of the treatment and goes back to baseline levels after prolonged suspension of omalizumab.^{2,5,6} The ABPA relapse treatment for patients with CF should be considered as a therapeutic option when IgE baseline levels double and when the patient does not respond to antibiotic treatment.⁵ We recommend having CF patients undergo ABPA screenings either annually or during periods of exacerbations when they do not respond to antibiotic treatments.¹⁰ In ABPA cases that are diagnosed and treated early, symptoms may be reduced, pulmonary function may improve, lung damage may be prevented and unnecessary treatments may be avoided.^{5,10} Omalizumab is a good therapeutic option to treat ABPA in corticosteroid-dependant patients, patients with frequent episodes, and those who experience many side effects from glucocorticoids.^{1,2,5,9} In order to establish the efficacy and safety of omalizumab in ABPA treatment,^{1,2} it is necessary to conduct a double-blind, randomised, placebo-controlled study.

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Isabel Delgado Pecellín*, Esther Quintana Gallego,
Celeste Pedregal Solano, Carmen Calero Acuña

Unidad de Fibrosis Quística, Hospital Virgen del Rocío, Sevilla, Spain

* Corresponding author.

E-mail address: idelpe@gmail.com (I. Delgado Pecellín).