



Letter

Efficacy of omalizumab treatment in a man with occupational asthma and eosinophilic granulomatosis with polyangiitis

Omalizumab is a humanized monoclonal antibody that binds to free-circulating immunoglobulin E (IgE). Several studies have shown the clinical efficacy of omalizumab in severe, persistent allergic asthma, including occupational cases.¹

We report the case of a 52-year-old man who described several years of severe symptoms of asthma and was subsequently diagnosed with occupational asthma and eosinophilic granulomatosis with polyangiitis (EGPA).

The patient had been working at a restaurant, with exposure to raw fish, since he was 20 years old. Respiratory symptoms improved only partially when he was away from work on holiday, but worsened once he returned to work. In the year before our evaluation, the patient had 8 asthmatic exacerbations requiring emergency medical visits and hospitalization. For this reason, he was fired from his job, but a few weeks later he resumed working at a different restaurant (again with exposure to raw fish). At the time of the diagnosis, the patient presented with blood eosinophilia (1,000 cells/ μ L), paranasal sinus infiltrates, and nasal polyps on computed tomography scan, and pulmonary infiltrates on chest x-ray. Other infectious parasitic causes of eosinophilia were excluded through our diagnostic work-up.

Eosinophilia fluid (>10%) was recorded on bronchoalveolar lavage assessment. Nasal cytology was performed by obtaining a nasal scraping from the middle portion of the inferior turbinate, using a Rhino-probe. The cellular forms of rhinitis were shown based on this cytotype, commonly referred to as “nonallergic rhinitis with eosinophils and mast cells” (eosinophils >20% and mast cells >10%).²

Fibrobronchoscopy with transbronchial biopsy showed a preserved pulmonary structure, with focal eosinophilic infiltration and evidence of mild to moderate vasculitis. Despite daily administration of high-dose inhaled combined beclomethasone/formoterol (800/24 μ g), montelukast tablet (10 mg), methotrexate (15 mg/wk), and oral methylprednisolone (25 mg), the patient had exacerbation of asthma when working at the fish restaurant.

When he came to our clinic, about 6 months after the EGPA diagnosis, pulmonary function tests demonstrated forced expiratory volume in 1 second/forced vital capacity (FEV₁/FVC) <70% and prebronchodilator FEV₁ <80% of predicted. The fraction of exhaled nitric oxide (NioxMino; Aerocrine AB, Solna, Sweden) was 290 parts per billion, so the patient met the Global Initiative for Asthma definition of severe, persistent asthma. No further EGPA clinical symptoms or signs were identified.

At the beginning of allergy work-up, the preliminary blood test confirmed eosinophilia (1,200 cells/ μ L). Skin-prick tests and serum-specific IgE assays (ImmunoCAP; Phadia, now Thermo Fisher

Table 1
Blood Test and Respiratory Function Data

	Value	
Examination	Before omalizumab	After omalizumab 1 year
FEV ₁	78%	95%
Total IgE	647 kU/L	230 kU/L
Specific IgE to AS	9.47 kUA/L	2.8 kUA/L
AQLQ	2.88	5.81
ACT	8	22
Eosinophils	23%	7%
CD4:CD8 ratio	1.90	1.40

Abbreviations: ACT, Asthma Control Test; AQLQ, Asthma-related Quality of Life Questionnaire; AS, *Anisakis simplex*; FEV₁, forced expiratory volume in 1 second; IgE, immunoglobulin E.

Scientific, Uppsala, Sweden) for the main inhalant allergens (house dust mites, cat dander, grasses, *Parietaria judaica*, cypress, *Aspergillus fumigatus*, *Cladosporium herbarium*, *Alternaria tenuis*), as well as for fish and seafood (codfish, sole fish, shrimp, lobster, gilt-head bream, and mussel), were negative. However, findings were positive for *Anisakis simplex* (AS), showing wheal with maximum diameter of 4 mm, surrounded by erythema 20 minutes after the skin-prick test, and 9.47 kUA/L on ImmunoCAP assay. Skin-prick testing with histamine (10 mg/mL) produced a wheal with a maximum diameter of 6 mm. In addition, we monitored inflammatory cells and cytokine expression in the peripheral blood before and after 12 months of therapy (Table 1).

Taking into account body weight (76 kg) and total serum IgE level at baseline (627 kU/L), a dose of 450 mg omalizumab was administered subcutaneously twice a month, after the patient's written informed consent. Each time he received a dose of omalizumab, we recorded manifestations related to disease progress (FEV₁, peak expiratory flow) and fraction of exhaled nitric oxide. Asthma-related Quality of Life Questionnaire scores, as determined by the Juniper questionnaire, were assessed before treatment and after 16 and 52 weeks.³ The Asthma Control Test, a validated self-administered tool to assess asthma control, was administered at the beginning of the treatment and then every month.⁴

Oral methylprednisolone was tapered (4 mg/wk) after 8 weeks and no further emergency visits were recorded. The overall Asthma-related Quality of Life Questionnaire score increased from 2.88 (before treatment) to 5.81 at week 52. The Asthma Control Test score increased from 8 (before treatment) to 22 at week 52. The CD4:CD8 ratio decreased to 1.40 at week 52. Eosinophils decreased from 23% to 7% at week 52. Nasal cytology performed after the treatment was normal and showed no inflammatory cells (neither eosinophils nor mast cells).

Disclosures: Authors have nothing to disclose.

<https://doi.org/10.1016/j.anai.2017.10.034>

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Therapy with omalizumab was well tolerated and the patient reported no asthmatic symptoms and no changes in work productivity or activity. FEV₁ values (% predicted) increased progressively during treatment, reaching reference normal values (up to 98%) after 8 months, and remained unchanged despite interruption of the inhalation therapy. Specific IgE for AS was progressively reduced to 2.8 kU/L, and total IgE at week 52 was 230 kU/L. No emergency department or medical visits or hospitalizations occurred during the treatment. An improvement of vasculitis symptoms was reported, as demonstrated by the lack of exacerbation of chronic rhinosinusitis and the reduction in CD score and symptoms.

As far as we know, only 1 previous case of occupational asthma caused by inhalation of AS allergens has been reported.⁵ The patient described herein had improved quality of life, returned to work, avoided further hospitalizations and exacerbations of disease during the 24-month follow-up, and no longer required oral corticosteroids.

As also observed by Giavina Bianchi et al,⁶ in a single patient, and by Spina and Miadonna,⁷ in patients with EGPA with uncontrolled asthma, our patient improved after omalizumab treatment without an increase in EGPA clinical severity—in contrast to findings by Winchester et al⁸ and Cisneros et al,⁹ who identified clinical manifestations of EGPA in their patients during treatment with omalizumab. We did not use mepolizumab (an anti-interleukin-5 drug) because it was not available in Italy at the time of the diagnosis.

A definitive diagnosis of professional sensitization cannot be made without performing a bronchial provocation test; however, with our patient, a strongly suggestive history together with a positive AS test suggested allergens of AS as being the cause of the reactions. The profession of restaurant worker is another factor to consider with regard to occupational allergy to AS.

Omalizumab represents an effective option for treating moderate to severe persistent allergic asthma, which can minimize the burden of systemic corticosteroids. While taking omalizumab, our patient exhibited improved asthma control (ie, reduced asthmatic reactions and a decreased risk of exacerbations). However, further studies on occupational IgE-mediated asthma are

required, especially when allergen exposure in the workplace cannot be avoided.

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