Omalizumab: a novel steroid sparing agent in eosinophilic granulomatosis with polyangiitis?

Sirs,

Bronchial asthma is one of the key features of the Eosinophilic Granulomatosis with Polyangiitis (EGPA/Churg-Strauss) (1, 2). In the vast majority of cases it is a chronic, steroid-dependent asthma, difficult-to-control despite the combination of inhaled high-dose corticosteroids and long-acting beta-2 agonists. Recently, in order to reduce the iatrogenic damage resulting from the long-term use of oral glucocorticoids, the use of steroid-sparing drugs has been widely recommended (3-6).

Omalizumab, a novel humanised monoclonal antibody that binds human IgE, has been now approved for the treatment of patients with moderate-to-severe persistent asthma of an allergic nature (7). As a systemic anti-IgE agent, the administration of omalizumab has been consistently associated with a reduction of number and severity of asthma exacerbations, better symptom control, significant reductions in corticosteroid dose, and improvement in patients' quality of life (8-11).

Controversial data have been reported on the efficacy and safety of omalizumab in EGPA (Table I). Similarly to leukotriene receptor antagonist, it remains unclear whether this drug may directly cause the vasculitis or only unmask a preexisting disease due to corticosteroid withdrawal (12-18).

Herewith, we propose the case of a patient, currently 38 years old, who came to our observation at the end of 2007 for a recent onset severe asthma with nasal polyps recurred after surgery. During the following two years, in spite of treatment with oral steroids for asthma control, he developed a persistent blood eosinophilia (eosinophil peak >14%) with pulmonary infiltrates to chest x-ray. The percentage of eosinophils in the induced sputum was 20%. Serum IgE were 246/uL IgE and skin prick test and serum specific IgE (RAST) were negative. Although the search for antineutrophil cytoplasmic antibody (ANCA) yielded negative results, the patient fulfilled the criteria for EGPA defined by the American College of Rheumatology (ACR) (19). Accordingly, he was treated with high-dose intravenous steroid pulses and azathioprine obtaining a complete remission of the lung infiltrates but only a partial control of rhinitis and asthma. Afterwards, despite several different immunosuppressive drugs were introduced as potential steroids sparing agents including methotrexate, cyclosporine and IvIg, it was never possible to reduce the daily dose of oral steroids below the threshold of 12 mg/day. On the contrary, during the follow-up, glucocorticoids were even increased due to the frequent asthma exacerbation episodes which led the patient to be admitted to the Emergency Department three times from 2009 to 2011. Figure 1 shows the sputum eosinophils, FEV1 and the oral corticosteroid dose during the follow-up. It was noteworthy that peripheral blood eosinophils, serum eosinophil cationic protein, IL-2, IL-4, IL-5 and ANCA remained normal or negative over the time. In August 2011, omalizumab (300 mg/every other week) was initiated. At the baseline assessment the patient had poor asthma control, with mild airway obstruction (FEV1/SVC 80% predicted; FEV1 75% predicted) and marked bronchial hyperreactivity (PD20FEV1 59 mcg), sputum eosinophils percentage was 36,18%, the FeNO was 44 ppb, total IgE were 66 UI/mL. During the following six months, the patient dramatically improved as reflected by both sputum eosinophil percentages and FEV1, while the dose of oral corticosteroid was gradually reduced and completely stopped by February 2012 (Fig. 1). To date,

Table I. Controversy about the use of omalizumab in EGPA.

Authors	n. of pts described	Impact on
EGPA (positive/negative)		
Giavina Bianchi P. *et al*. (2007)	1	Positive
Pabst S. *et al*. (2008)	2	Positive
Puechal X. *et al*. (2007)	1	Negative
Bargagli E. *et al*. (2008)	1	Negative
Ruppert A.M. *et al*. (2008)	1	Negative
Spina M.F. *et al*. (2009)	1	Negative

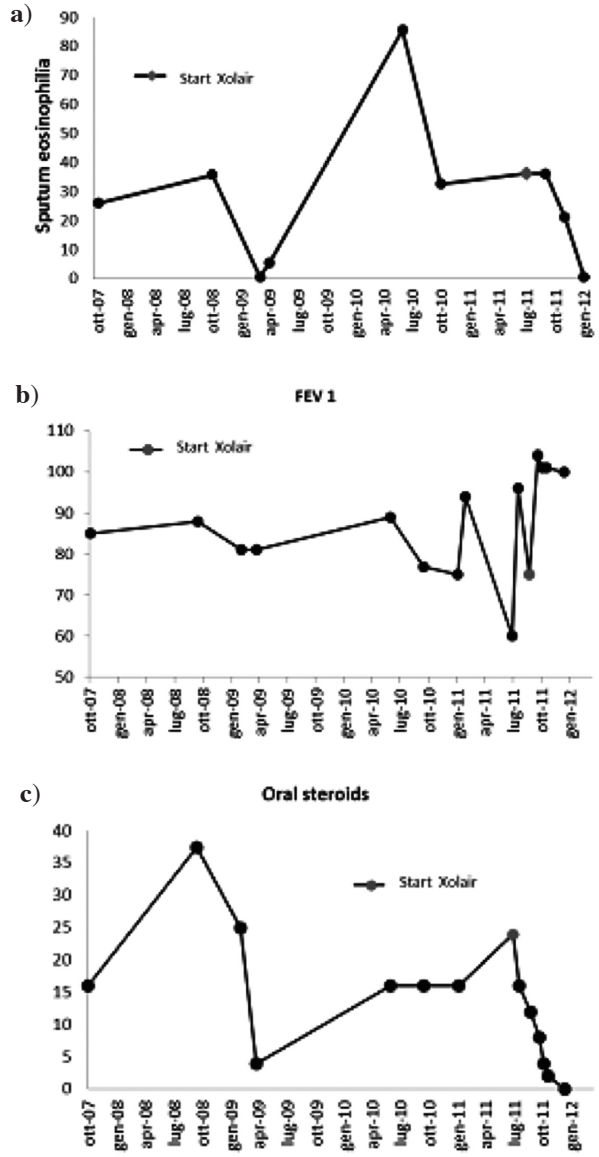

Fig 1.
a) Sputum eosinophil percentages
b) FEV1
c) dose of oral corticosteroid

the disease is in remission and the patient has reached a satisfactory asthma control, with only one episode of asthma exacerbation which required a transient short course of prednisone. At the moment, the patient refers a remarkable improvement of his quality of life, with a significant weight loss and a reduction of the number of the working days lost due to illness.

In summary, this clinical case supports the use of omalizumab in patients with EGPA even in the absence of atopy. Other reports have already described that omalizumab may be safely and successfully used in EGPA (14, 20). This report particularly emphasises the possibility that omalizumab may contribute to asthma control not only through the classical anti-IgE mechanism but also through a direct effect on the eosinophilic bronchial inflammation shedding new lights on the potential mechanisms of action of this novel drug. Interestingly, omalizumab allowed the patient to completely withdraw the oral corticosteroids, a goal that he had never reached before by using traditional immunosuppressive drugs. From this point of view then, this case outlines the importance of a targeted treatment in EGPA patients to achieve and maintain clinical remission over the time thus reducing the disease societal impact and its healthcare resource consumption (21). Traditional immunosuppressive treatments may control the systemic activity of the vasculitis but may be not sufficient to control the asthma symptoms or the ENT involvement. Thus, concerted efforts towards multidisciplinary targeted therapy in EGPA seem strongly desirable.

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