

SITs were 6 *Polistes dominulus* (Anallergo, Florence, Italy), 8 *Vespa germanica*, 1 *Polistes* spp, and 1 *Apis mellifera* (Stallergenes, Antony, France).

Two patients had reactions during the build-up phase of immunotherapy. One (patient 6) had generalized pruritus without skin lesions or other signs, and one (patient 9) had a grade I urticaria. In both cases, the dose escalation was temporarily stopped by repeating the last tolerated dose, and a premedication with cetirizine 10 mg was given. After 2 weeks, the patients could resume the build-up and reach the maintenance dose without further reactions. Thirteen patients received 1 or more *Hymenoptera* sting on-field during the maintenance phase, and only 2 of them (patient 3 and patient 14) had a grade IV reaction at the first resting. In these patients, the dose was safely increased to 200 µg, and at subsequent stings they had only a mild local reaction. In the remaining 11 patients, only mild local reactions were seen at re-sting.

On the basis of the current literature, SM is considered a high-risk situation for SIT in HVA, because severe events or fatalities can occur.^{3,5} Nonetheless, these patients are also at very high risk when they are stung by the sensitizing *Hymenoptera*.^{2,3} and SIT can confer a satisfactory protection. On the basis of these considerations and previous clinical observations,⁶ we vaccinated several patients with SM without observing important side effects. Moreover, almost all of them achieved a relevant protection and decreased their grade of reaction from IV to I. The 2 patients who maintained a grade IV reaction on maintenance SIT could achieve a benefit by increasing the maintenance dose.⁸ We are aware that the population evaluated in our study is small, but if we take into account the rarity of SM and the low frequency of severe HVA, this study includes the largest cohorts of patients with HVA and SM treated with SIT. An accessory observation is that SM was indeed diagnosed in 16 of 121 patients with severe HVA. Thus it can be supposed that severe HVA could be a clinical manifestation of underlying SM, as reported with idiopathic anaphylaxis.⁹ This would support the usefulness of tryptase assay screening in patients with *Hymenoptera*-induced anaphylaxis. On the basis of the observed risk/benefit ratio, we suggest that patients with ascertained SM and HVA receive a specific vaccination with a very slow increase of the dose, carefully respecting the recommendations for a safe administration.

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Anti-IgE (omalizumab): A new therapeutic approach for chronic rhinosinusitis

To the Editor:

Chronic rhinosinusitis is a common but poorly defined disease characterized by inflammation of nasal mucosa and paranasal sinuses. Approximately 16% of the US population is affected.¹ Etiology and pathophysiology of chronic rhinosinusitis are unknown as yet. Allergic inflammation, mucociliary dysfunction, aspirin intolerance, immunodeficiency, cystic fibrosis, and nasal and paranasal sinus infections are discussed as relevant factors or underlying diseases. Chronic rhinosinusitis is known to be a notoriously difficult-to-treat disease, and established therapies are often ineffective.²

We provide preliminary data indicating anti-IgE may have efficacy in the treatment of refractory chronic rhinosinusitis.

A 68-year-old patient has a 20-year history of chronic rhinosinusitis, nasal polyposis, persistent asthma, and aspirin intolerance. Asthma was treated with inhaled corticosteroids and long-acting β₂-agonists. Therapies with antibiotics, antihistamines, corticosteroids (topically and systemically), and montelukast had been ineffective for his chronic rhinosinusitis. Each of 5 previous sinus surgeries was shortly followed by a relapse. When the patient was referred to our department in 2004, he had severe persistent rhinitis with persistent nasal obstruction, postnasal drip, relapsing bacterial nasal and sinus infections, and absence of sense of smell and taste. In spite of daily use of high dose inhaled fluticasone and salmeterol, asthma symptoms affected his activity and sleep. FEV₁ was decreased at 78.4% (2.76 L), and forced vital capacity was normal at 88.2% (4.03 L), according to Global Initiative for Asthma (GINA) III.^{3,4} Skin prick tests showed a positive reaction only to house dust mite extract. Total serum IgE level as well as the specific IgE to house dust mite were elevated. A nasal challenge with house dust mite extract induced severe secretion, mucosal swelling, and total obstruction analyzed by rhinomanometry. Asthma symptoms and history met the criteria for anti-IgE therapy. In addition, a severe chronic polypoid sinusitis with subtotal swelling and inflammation of the entire paranasal sinus associated with

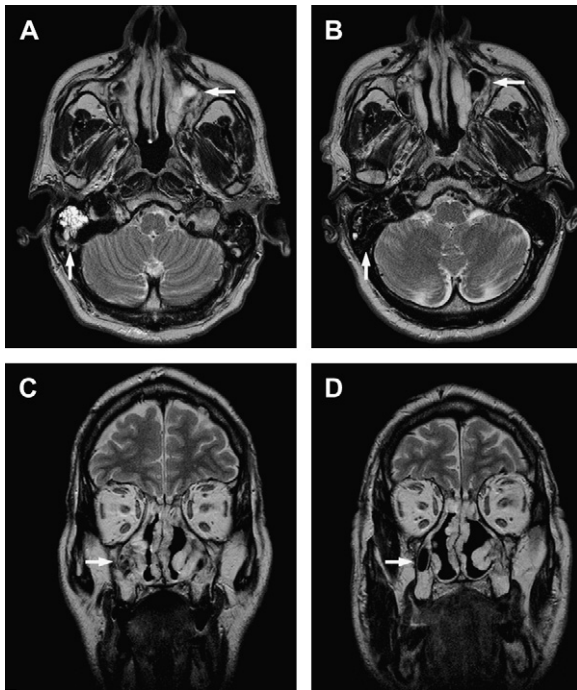


FIG 1. MRI scans demonstrate the improvement of mastoiditis, sinus ventilation, and mucosal edema after anti-IgE treatment (**B, D**) in contrast with pretreatment MRI (**A, C**). The reduction of mucosa swelling and the increase of nasal patency enables the patient to undergo a 20-minute closed-mouth scan without any difficulties (**D**), in contrast with the open-mouth scan necessary for the pretreatment condition (**C**).

a chronic but asymptomatic mastoiditis was diagnosed by magnetic resonance imaging (MRI; Fig 1).

Hence, in 2006 we initiated a therapy with 225 mg omalizumab biweekly (calculated for a body weight of 83 kg and total serum IgE level of 216 kU/L). Asthma symptoms clearly ameliorated within 2 months, and the patient reported a significant reduction of his sinus complaint. Chronic forehead and paranasal pressure as well as retronasal mucus were eliminated, and his sense of smell was restored. Four months after therapy initiation, a resolution of nasal mucosa swelling and a reduction of polypoid swelling and inflammation of the entire paranasal sinus were documented by MRI. The chronic mastoiditis had been completely eliminated (Fig 1). Thus MRI scan results coincide with the patient's report. Although computed tomography scans are the typical approach for the diagnosis of chronic rhinosinusitis, MRI scans were conducted in this case because of the lower radiation exposure with repeated examination.

Omalizumab is a humanized anti-IgE antibody approved for treatment of moderate to severe persistent asthma when a positive skin test or *in vitro* reactivity to a perennial aeroallergen is documented, and if symptoms are inadequately controlled by inhaled corticosteroids and inhaled long-acting β_2 -agonists.⁵ The efficacy of omalizumab has been clearly demonstrated for this indication by several clinical studies.⁶ Furthermore, the benefit of omalizumab for patients with allergic asthma and associated allergic rhinitis has been demonstrated in the Study of Omalizumab in Comorbid Asthma and Rhinitis (SOLAR).⁷

Our report suggests that omalizumab can be effective in the treatment of chronic rhinosinusitis. We observed not only a resolution of nasal mucosa swelling (in accordance with the

SOLAR study) but also a reduction of polypoid swelling and inflammation of the entire paranasal sinuses, and a complete healing of chronic mastoiditis. The anti-IgE therapy reduces the allergic inflammation, and our case report gives further evidence for an IgE-mediated mechanism (IgE antibodies to bacterial superantigens and aeroallergens) in the pathophysiology of chronic rhinosinusitis at least in some patients. To broaden the therapeutic applications of omalizumab, further studies must be conducted.

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The effect of etanercept on the human cutaneous allergic response

To the Editor:

Etanercept (Enbrel; Immunex Corp, Thousand Oaks, Calif) is a TNF receptor 2-Fc fusion protein approved for the treatment of rheumatoid arthritis, juvenile rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, and psoriasis. It antagonizes the actions of both TNF- α and TNF- β , but most of its clinical efficacy is the consequence of TNF- α antagonism. TNF- α is a potent multifunctional cytokine produced by a wide variety of cell types and is important for host defense and inflammatory cell influx and activation.¹ Recent studies have demonstrated that TNF- α levels are elevated in the lungs of patients with severe asthma, and neutralizing its activity may be an effective treatment.²⁻⁴ To date, however, no human studies have been conducted to explore the effect of TNF- α inhibition on allergic inflammation in the skin. We conducted this open trial to determine whether systemic administration of etanercept at doses effective for psoriasis could affect allergic responses in the skin.