

description of anaphylactic reactions with multiple allergens (1, 2), although in these reports, more than three unrelated allergens (nonstandardized in one case) were used. In the population herein considered, no difference in the type and characteristics of side-effects was seen according to the number of allergens used (one or two). The overall number of patients is relatively small, but the reliability of the data is supported by the concordance of the figures with those reported in larger samples (3–5). Our conclusion is that SLIT with a limited number of mixed allergens does not increase the risk of side-effects, if the treatment is correctly prescribed and standardized extracts are used.

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High omalizumab dose controls recurrent reactions to venom immunotherapy in indolent systemic mastocytosis

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Key words: Hymenoptera; immunotherapy; mastocytosis; Omalizumab; venom.

Pure venom immunotherapy (VImRx) is associated with adverse reactions, particularly in individuals with mastocytosis, occasionally leading to treatment withdrawal (1). The present report refers to a patient suffering from indolent systemic mastocytosis and multiple reactions during VImRx; his treatment progressed without further adverse events on high-dose omalizumab pretherapy, administered 1 week to 1 h earlier.

N.A., a 45-year-old man, with a near fatal anaphylactic reaction to a bee sting, was observed to suffer from indolent systemic mastocytosis [serum tryptase (42.5 µg/l, UniCAP Tryptase Pharmacia/Upjohn), a positive Tc99m-MDP bone scan, as well as bone marrow biopsy]. Allergological evaluation (IDST and RAST; Unicap Pharmacia/Upjohn) confirmed IgE sensitization to bee venom ($W = 12 \times 25$, $F = 40 \times 70$ at 0.01 µg/ml vs histamine 10×18 , 60×78 mm, respectively).

An inpatient modified rush VImRx scheme was initiated and patient was

placed on H1 and H2 antagonist (Levocetirizine, cetirizine, dimethindene at 8-h intervals and ranitidine every 12 h.) for prophylaxis because of frequent adverse reactions. VImRx was progressed slowly to a cumulative dose of 150–200 µg in three to four divided doses at 28-day intervals. Mild-to-moderate reactions occurred 20- to 30-min postinjection in all but one, session; when there was a severe one at 18 months of VImRx that led to a trial of omalizumab; patient gave written informed consent.

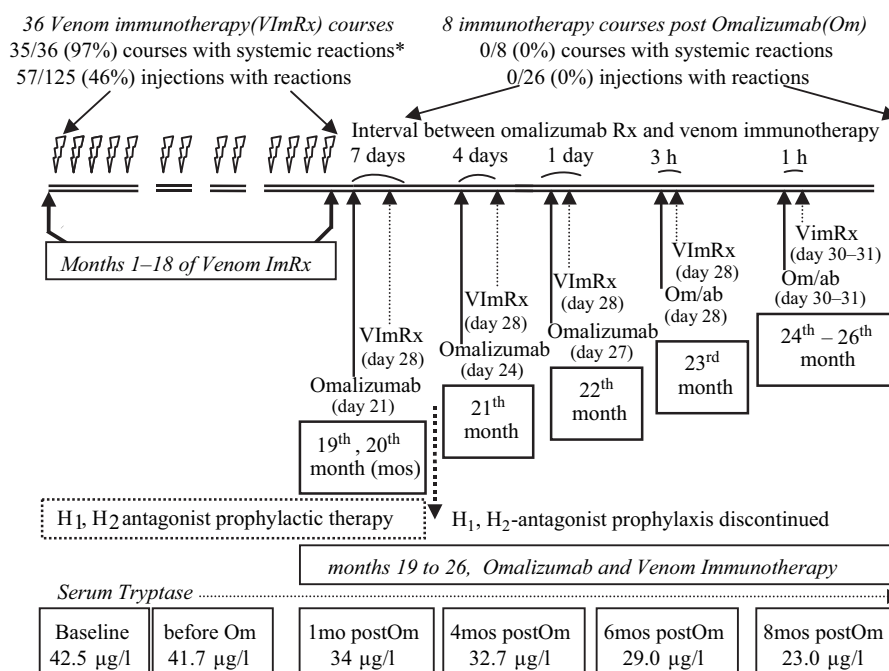
One week prior to the subsequent monthly schedule of VImRx course, the patient received 300 mg omalizumab s.c. – twice the recommended dose based on weight (84 kg) and IgE (62 KU/ml) – without adverse events. Seven days later, he tolerated a cumulative dose of 150 µg venom (double the previous month's reduced dose) without any reaction. The same procedure was repeated successfully a month later and H1–H2 antagonists were discontinued. Omalizumab was administered at progressively shorter intervals, until 1 h between the two treatments was reached (Fig. 1). Patient tolerated the single 100 µg maintenance dose (never achieved before) without adverse events.

Serum tryptase measurements showed a progressive reduction (Fig. 1) and IDST, repeated at 8 months, 3×2 mm erythema at 1 µg/ml of venom. Two and three weeks later patient tolerated single stings by unknown Hymenoptera. Heat-induced flushing – the only subjective complaint of mastocytosis – ceased to be a problem, even at temperatures exceeding 45°C.

Omalizumab, the humanized m-anti-body to the Fcε, blocks the binding of free IgE to its corresponding FcεRI on basophil and mast cells, thus inhibiting their activation by allergens. Furthermore, it causes rapid reduction in the FcεRI expression by basophils (2) and a slower one by dermal mast cells (3), while it exerts additional immune-modifying effects.

Omalizumab, administered 9 weeks before rush pollen immunotherapy, significantly reduced reactions (4), while unprovoked anaphylaxis was aborted in two systemic mastocytosis patients (5).

High dose, 7-day to 1-h omalizumab pretreatment controls recurrent venom immunotherapy reactions in mastocytosis.



* **43 mild:** flushing facial or more generalized, tachycardia ± eye injection, nasal obstruction.

Required Rx: IV Normal Saline (NS) infusion, close observation

13 moderate: above findings, plus drop in BP ± nausea.

Required Rx: as above plus a single adrenaline dose (0.3mg) SC.

1 severe: above plus weak pulses, marked drop in BP despite rapid NS infusion IV, nausea, vomiting, diaphoresis; Required Rx: above, >1adrenaline dose + corticosteroids IV.

Figure 1. Time course of venom immunotherapy before and after omalizumab treatment, observed adverse reactions and serum tryptase levels in patient NA with indolent systemic mastocytosis.

A single case-report suggests the protective effect of Omalizumab against VImRx reactions (6).

The present case represents the first report on combining omalizumab with specific immunotherapy to improve the safety of the latter in mastocytosis patients.

When omalizumab treatment was initiated in our patient, it was hypothesized that a higher than the recommended dose would be required for efficacious down-regulation of FcεRI expression on pathologically increased numbers of mast cells. The 7-day interval between the two treatments was chosen, because of the reported reduced responses to allergens as early as one week post-Omalizumab (3). However, shorter intervals – up to 1 h – were gradually applied with success, making the combined therapy more convenient.

The continuous decline in serum tryptase over 8 months noted in our case had

not been observed in the two mastocytosis cases reported by Carter et al. (5), who received the recommended for asthma dose over 24 months. The dose at double the levels administered to our patient might account for the observed difference.

Our search of the literature failed to identify previous reports on Omalizumab in mastocytotic venom immunotherapy reactors; further studies are required with emphasis on dose response.

The author wishes to thank Mr and Mrs N.A. for their patience and confidence in our treatment options. Dr Michael Makris's (presently at Allergy Unit, Attikon Un. Hospital, Athens, Greece) help during the first year of VImRx is also recognized.

No financial or other relations with the manufacturing company of either drug used in the present case.

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A variant of idiopathic angioedema presenting as persistent facial swelling over 1 year

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Key words: angioedema; facial swelling; skin biopsy.

Angioedema is characterized by swelling of the deeper layer of the skin and/or the submucosa. It is usually localized,

sudden, and transient, lasting from several hours to a few days and is often recurrent. The swellings develop

from extravasation of plasma in the affected areas because of a transient increase in endothelial permeability caused by vasoactive substances produced locally (1). Histopathologically, it presents as localized edema with separation of collagen fibers and blunting and widening of the rete pegs, along with the presence of mast cells and eosinophils (2). We describe here a patient with chronic angioedema that persisted for over 1 year.

A 32-year-old woman visited the allergy clinic for prolonged facial swell-

Idiopathic angioedema presenting as persistent facial swelling over 1 year.

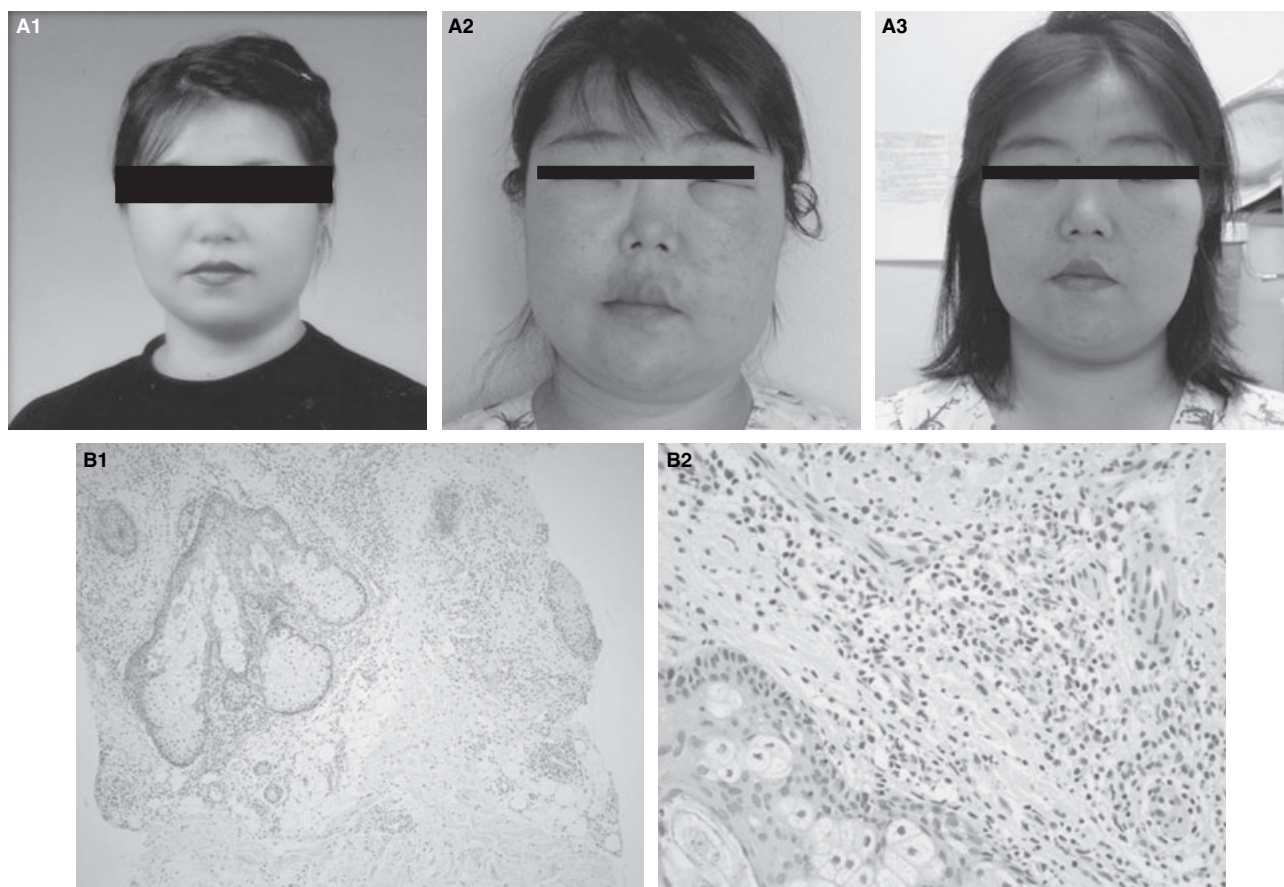


Figure 1. (A) A 32-year-old woman with prolonged facial swelling lasting over 1 year. (A-1) Before development of the disease. (A-2) At time of admission. (A-3) After treatment with high dose steroids. (B) A skin biopsy specimen showing dense lymphocytic infiltration in the deep dermis, particularly in the periappendageal and perivascular areas. (B-1) Hematoxylin–eosin staining; original magnification ×100. (B-2) Hematoxylin–eosin staining; original magnification ×400.