Eur Ann Allergy Clin Immunol Vol 49, N 3, 143-144, 2017

R. Asero

Disappearance of severe oral allergy syndrome following omalizumab treatment

Ambulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano, Italy

Key words
food allergy; IgE; omalizumab; oral allergy syndrome; treatment

Summary
The first case of disappearance of apple-induced oral allergy syndrome in a birch pollen-allergic patient following omalizumab treatment is reported. This observation in a case of type 2 food allergy suggests that omalizumab is potentially an effective preventive treatment for patients with severe, type 1 food allergies.

Corresponding author
Riccardo Asero
Ambulatorio di Allergologia,
Clinica San Carlo
Via Ospedale 21
20037 Paderno Dugnano (MI), Italy
E-mail: r.asero@libero.it

Introduction

It has long been known that birch pollen-allergic patients frequently develop oral itching with angioedema of the lips following the ingestion of fresh foods and vegetables, due to the presence of allergen proteins homologous to the major birch pollen allergen, Bet v 1. This phenomenon is known as oral allergy syndrome (OAS). Although in most cases limited to the oral cavity, reactions may be sometimes severe enough to involve the pharynx and to prevent patients to eat a large spectrum of fresh and raw fruits and vegetables, with a significant reduction of their quality of life. The apple is the fruit most frequently involved in such food allergies, due to the very high homology of its PR-10 allergen, Mal d 1, with Bet v 1 (1-4). Previous studies showed that allergen immunotherapy with birch pollen extracts may reduce or abolish secondary apple allergy (revised in [5]).

Omalizumab, a humanized anti-IgE monoclonal antibody indicated for a long time in severe cases of allergic asthma, has been recently introduced also as a treatment for patients with refractory chronic urticaria. Omalizumab binds the Fc3 subunit of free IgE molecules and it is generally accepted that the reduced binding of free specific IgE to the high affinity IgE receptor (FceRI) eventually leads to a reduced density of specific IgE on the surface of mastcells and basophils, and to the down-regulation of the receptor itself. In food allergy, omalizumab has been experimentally tried in cases of severe allergies both as a monotherapy (mainly in adults) (6-8) and as an add-on treatment to oral immunotherapy (OIT; virtually only in children) (9-12). In most cases, the drug was able to increase significantly the threshold dose of offending foods required to induce adverse reactions. No data about the effect of omalizumab in type 2 food allergies are available to date.

Case report

A 51-year old woman was seen at the allergy department of the Clinica San Carlo. She had suffered from severe generalized pruritus for more than 1 year, sometimes associated with the occurrence of itchy wheals. The skin complaints progressively worsened, with the occurrence of recurrent large wheals that no longer responded to second generation antihistamines, even at higher than licensed doses (levocetirizine 15 mg/day). At this time point, the Urticaria Activity Score (UAS-7) scored 32. The patient also had a 20-year history of seasonal springtime rhinoconjunctivitis, and reported severe OAS following the ingestion of *Rosaceae* (apple, peach, cherry, apricot, plum and almond), grapes, fennel, carrot, and kiwi. The ingestion of these fruits caused severe oral itching and tingling, and the rapid onset of angioedema of the lips and eyelids. The woman reported that the apple was by far the plant-derived food inducing the most severe reactions. The patient underwent skin prick tests (SPT) with a large series of commercial extracts of airborne allergens (Allergopharma, Reinbeck, Germany) including pollens (grass, mugwort, ragweed, pellitory, plantain, birch, cypress and olive), house dust mites, Alternaria spp, and dog and cat dander. Birch and cypress pollen scored strongly positive (mean wheal diameter 12 mm), as did a SPT with fresh Golden Delicious apple by the Prick-Prick technique (10 mm). Both a SPT with commercial date palm, profilin-enriched, pollen extract (ALK-Abellò, Hørsholm, Denmark; 50 µg protein/ml) and a SPT with a commercial peach extract (ALK-Abellò; containing LTP 30 µg/ml), markers of profilin and lipid transfer protein hypersensitivity, respectively, scored negative. The level of specific IgE to birch pollen, measured by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden), was 12.6 kUA/L. Chronic spontaneous urticaria (CSU), resistant to antihistamines, was diagnosed, along with birch and cypress pollinosis and type 2, cross-reactive food allergy. In view of the severity of the CSU, after written informed consent was obtained from the patient, subcutaneous omalizumab 300 mg/month was started. Urticaria promptly and completely responded as short as 1 week after the first administration, and at month 3 of treatment, during the birch pollen season, an open challenge with a Golden Delicious apple was carried out. The woman was able to tolerate an entire apple without symptoms. At this point SPT with birch pollen extract and fresh Golden delicious apple were performed. While the former induced a wheal whose mean diameter was similar to that observed at the first visit (12 mm), the apple-induced wheal was much reduced (mean diameter 4 mm).

Conclusion

This is probably the first report on the effects of anti-IgE treatment on type 2 food allergy. It confirms the conclusions of studies on type 1 food allergies that omalizumab markedly increases the threshold dose of food allergen needed to elicit clinical symptoms. Looking at studies on chronic urticaria and bronchial asthma showing that the effect of the drug is short-lived, one can expect that the effect of omalizumab on food allergy vanishes in as short as two months once the drug is discontinued. Nonetheless, omalizumab seems to represent an effective preventive treatment for patients with severe food allergies.

References

1. Valenta R, Kraft D. Type I allergic reactions to plant-derived foods: a consequence of primary sensitization to pollen allergens. J Allergy Clin Immunol. 1996;97(4):893-8.
2. Ebner C, Birkner T, Valenta R, Rumpold H, Breitenbach M, Scheiner O, Kraft D. Common epitopes of birch pollen and apple. Studies by Western and Northern blot. J Allergy Clin Immunol. 1991;88(4):588-94.
3. Vieths S, Janek K, Aulepp H, Petersen A. Isolation and characterization of the 18 kDa major apple allergen and comparison with the major birch pollen allergen (Bet v 1). Allergy. 1995;50(5):421-30.
4. Vanek-Krebiz M, Hoffmann-Sommergruber K, Laimer da Camara Machado M, Ebner C, Kraft D, Scheiner O, Breiteneder H. Cloning and sequencing of Mal d 1, the major allergen from apple (Malus domestica), and its immunological relationship to Bet v 1 the major birch pollen allergen. Biochem Biophys Res Commun. 1995;214(2):538-51.
5. Asero R. Is there a role for birch pollen immunotherapy on concomitant food allergy? Curr Treat Options Allergy. 2015;2:83-9.
6. Leung DYM, Sampson HA, Yunginger JW, Burks AW, Schneider LC, Wortel CH, Davis FM, Hyun JD, Shanahan WR Jr; Avon Longitudinal Study of Parents and Children Study Team. Effect of Anti-IgE Therapy in Patients with Peanut Allergy. N Engl J Med. 2003;348(2):986-993.
7. Sampson HA, Leung DYM, Burks AW, Lack G, Bahna SL, Jones SM, Wong DA. A phase II, randomized, double-blind, parallel-group, placebo-controlled oral food challenge trial of Xolair (omalizumab) in peanut allergy. J Allergy Clin Immunol. 2011;127(5):1309-10.
8. Savage JH, Courneya J-P, Sterba PM, MacGlashan DW, Saini SS, Wood RA. Kinetics of mast cell, basophil, and oral food challenge responses in omalizumab-treated adults with peanut allergy. J Allergy Clin Immunol. 2012;130(5):1123-9.
9. Nadeau KC, Schneider LC, Hoyte L, Borras I, Umetsu DT. Rapid oral desensitization in combination with omalizumab therapy in patients with cow's milk allergy. J Allergy Clin Immunol. 2011;127(6):1622-4.
10. Schneider LC, Rachid R, LeBovidge J, Blood E, Mittal M, Umetsu DT. A pilot study of omalizumab to facilitate rapid oral desensitization in high-risk peanut-allergic patients. J Allergy Clin Immunol. 2013;132(6):1368-74.
11. Bégin P, Dominguez T, Wilson SP, Bacal L, Mehrotra A, Kausch B, Trela A, Tavassoli M, Hoyte E, O'Riordan G, Blakemore A, Seki S, Hamilton RG, Nadeau KC. Phase 1 results of safety and tolerability in a rush oral immunotherapy protocol to multiple foods using omalizumab. Allergy Asthma Clin Immunol. 2014;10(1):7.
12. Wood RA, Kim JS, Lindblad R, Nadeau K, Henning AK, Dawson P, Plaut M, Sampson HA. A randomized, double blind, placebo-controlled study of omalizumab combined with oral immunotherapy for the treatment of cow's milk allergy. J Allergy Clin Immunol. 2016;137(4):1103-10.