

Dupilumab for treatment of food allergy



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Clinical Implications

- This clinical communication provides evidence of treatment with dupilumab related to the acquisition of tolerance to a food that previously induced an allergic reaction.

TO THE EDITOR:

Dupilumab, a fully human monoclonal antibody against the α subunit of the IL-4 receptor that inhibits IL-4 and IL-13 signaling, was first approved by the Food and Drug Administration for use as a biologic treatment for atopic dermatitis (AD), and then in 2017 by the European Medicines Agency. Although this antibody is currently indicated for the treatment of moderate-to-severe AD in adult patients who are candidates for systemic treatment,¹ dupilumab also has proven effectiveness in treating severe and persistent asthma, and is being actively investigated as therapy for chronic rhinosinusitis with nasal polyposis and for eosinophilic esophagitis.^{2,3} To date, however, no studies have investigated its potential for use in IgE-mediated food allergy.

The most successful existing therapy is food oral immunotherapy, an approach that is not risk free and sometimes requires pretreatment with omalizumab for success.

Exposure to a food antigen induces IgE binding to mast cells and basophils, activating these cells and triggering the release of the inflammatory mediators responsible for tissue response and clinical symptoms. Intestinal mast cells produce IL-4, IL-13, IL-9, and Th2 chemokines that favor the recruitment of Th2 cells in the intestine that are responsible for recruiting and expanding intestinal mast cells.⁴ Therefore, inhibiting IL-4/IL-13 signaling is likely to reduce the recruitment of mast cells at the intestinal level, decreasing the clinical expression of food allergy.

We present a 30-year-old woman with a history of severe AD, allergic rhinitis without asthma due to grass, olive, and cypress pollen sensitization, and no symptoms related to food allergy. In August of 2017, the patient experienced anaphylactic shock (dyspnea, generalized urticaria, and hypotension) minutes after ingesting canned corn (previously she had tolerated it without incident), without any other triggering factors such as physical exertion or administration of nonsteroid anti-inflammatory drugs. An allergy workup included skin prick tests with a battery of several foods, producing positive results for peach, corn, peanut, almond, pistachio, sunflower seeds, hazelnut, and walnut. Specific IgE measured by ImmunoCAP (Termo Fisher, Uppsala, Sweden) showed positive results for rAra h 9, rCor a 8, rPru p 3, and corn extract. Based on these results, the patient was diagnosed with allergy to corn and to nuts with a positive lipid transfer protein pattern. As the patient did not know if she tolerated *Rosaceae* fruits and nuts, it was recommended to avoid corn, *Rosaceae* fruits, and nuts. An open food challenge test was carried out in November

2017, resulting in good tolerance to a common portion of sunflower seeds and almonds. However, the patient developed generalized urticaria within 10 minutes of ingesting 2 pistachios. After this test, the patient was recommended to avoid pistachio and cashew and resume intake of sunflower seeds and almonds. In December 2017, the patient began treatment with dupilumab due to severe AD (SCORAD score, 88) and a previous poor response to ciclosporin. The patient received an initial dose of 600 mg, followed by 300 mg every 2 weeks. After 1 month of treatment, an improvement was observed in her dermatitis (SCORAD score, 65). After 3 months of treatment with dupilumab, continued improvement in dermatitis was seen (SCORAD 50). The patient reported having inadvertently eaten some pistachios in a salad, though without adverse reaction. Given these findings, we decided to perform an oral challenge test with pistachios, reaching a quantity of 50 g of pistachios without no immediate or delayed reactions. Two weeks later, during an outpatient visit for administration of dupilumab, she reported having eaten canned corn at home (4 kernels of corn) without developing a reaction. An agreement was reached with the patient to perform a challenge test with canned corn (the same one that had caused the reaction in August 2017) in a hospital environment, reaching a highest tolerated dose of 100 g without any immediate or delayed adverse reactions. Given that the only element that varied between the reaction to corn in August 2017 and her response to the pistachio challenge in November 2017 was the introduction of dupilumab, it appears that administration of this antibody has aided the patient in acquiring tolerance to the food.

In conclusion, we report a patient with severe AD and food allergy who, after initiating treatment with dupilumab, has come to tolerate 2 foods that induced previous allergic reactions, with this tolerance being confirmed by oral challenge. To our knowledge, this is the first case providing evidence of treatment with dupilumab related to the acquisition of tolerance to a food that previously induced an allergic reaction, and as such can serve as proof of concept for the development of new lines of research in this field. No clinical trials have been undertaken to study the use of dupilumab as a treatment for food allergy,⁵ a disease with very few therapeutic options.

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