

## Letter to the Editor

**Successful use of omalizumab for prevention of fire ant anaphylaxis**

To the Editor:

Imported fire ant (IFA) anaphylaxis is a common cause of insect sting anaphylaxis in the United States, accounting for the majority of insect hypersensitivity in the southeastern United States (including Texas).<sup>1</sup> Standard and rush immunotherapy with IFA whole-body extract (WBE) have been used successfully for the prevention of subsequent anaphylaxis in patients with allergy.<sup>2,3</sup> The current standard of care for individuals with systemic reactions to IFA stings is WBE immunotherapy at a maintenance dose of 0.5 mL of a 1:100 wt/vol with higher dosing considered for the rare treatment failures.<sup>4</sup> We report a case of a patient who failed to respond to higher than conventional doses of IFA WBE immunotherapy who was treated with omalizumab with protection against subsequent IFA sting reactions.

A 32-year-old woman was referred for evaluation of a systemic reaction to IFA. She is a native Texan and previously had large local reactions to fire ant stings. Her past medical history was significant only for mild seasonal allergic rhinitis. Her initial systemic reaction occurred at the age of 30 years while walking barefoot outdoors. She had multiple IFA stings on her feet and developed itchy palms, lightheadedness, and dyspnea within 10 minutes. She was rushed to the emergency department, had documented hypotension, and was treated with antihistamines and corticosteroids with eventual recovery. A skin prick test to 1:10 wt/vol IFA WBE was positive 6 weeks after the reaction with a 3 × 4-mm wheal with flare. She underwent a successful 2-day rush desensitization starting with 0.1 mL 1:100,000 wt/vol and progressing to 0.5 mL 1:1000 wt/vol on day 1. On day 2, she was started on 0.1 mL 1:100 wt/vol and advanced up to 0.3 mL 1:10 wt/vol (stock bottle) of IFA WBE mix (*Solenopsis invicta/richteri*; Hollister-Stier, Spokane, Wash) with no reaction over the 2-day period. It is the standard of practice at this institution to use 0.3 mL 1:10 wt/vol as a maintenance dose because of the inherent variability in potency of WBE. After 8 months of monthly immunotherapy, she sustained an IFA field sting to her bare foot with pustule formation. Within minutes, she developed dizziness, palpitations, throat tightness, and palmar itching. Epinephrine was administered by her brother, and she was transported to the emergency department with eventual resolution of her symptoms. Two weeks after this reaction, an attempt to reinstate her immunotherapy (4 weeks after the last administration of her maintenance dose) with 0.2 mL of 1:10 wt/vol was made with the intent of raising the dose; however, this resulted in a systemic reaction 7 minutes after receiving the injection. She developed hypotensive anaphylaxis with facial flushing, dizziness, and dyspnea, with a blood pressure of 72/40 mm Hg and pulse of 120 beats/minute. Treatment with multiple injections of epinephrine (a total of 0.8 mg) intramuscularly in the thigh resolved her symptoms. Her total tryptase obtained acutely was elevated at 22 ng/mL (with her baseline level 8.75 ng/mL and normal <11.5 ng/mL).

On the basis of her anaphylactic reactions to both a field sting (subjective) and an IFA immunotherapy injection (documented) after 8 months of high-dose immunotherapy, she was determined to be an immunotherapy treatment failure. Furthermore, the

patient was very hesitant to restart immunotherapy. A trial of anti-IgE therapy with omalizumab was therefore discussed with the patient as a potential therapy for her life-threatening anaphylaxis because she failed to respond to high-dose IFA WBE immunotherapy. She was subsequently initiated at 150 mg subcutaneously monthly, with dosing based on body weight (61 kg) and her serum total IgE level (40 IU/mL) according to asthma dosing guidelines. Omalizumab was well tolerated without adverse reactions. After 8 doses, the patient underwent an intentional sting challenge with 2 separate IFA stings without systemic reaction. Another intentional sting challenge with 2 separate IFA stings was performed after 51 months of omalizumab, and she developed palmar pruritus and a local wheal (15 mm) and flare (9 mm) response but no systemic symptoms. Furthermore, she has sustained 4 separate IFA field stings each 12 to 24 months apart with no systemic reactions while on omalizumab. To date, our patient has received monthly omalizumab for 70 months with no complications related to omalizumab therapy. We plan to continue omalizumab therapy and perform periodic intentional sting challenges to document efficacy. The frequency and duration of this therapy is unknown currently because the long-term immunomodulatory effects of omalizumab are not known.

The typical maintenance dosage for IFA WBE immunotherapy is 0.5 mL 1:100 wt/vol extract, which contains 1.5 to 2.2 mg of Sol i 3 protein, the equivalent of approximately 19 IFA stings.<sup>5</sup> Our patient underwent a 2-day rush desensitization and received high maintenance doses of WBE immunotherapy (0.3 mL 1:10 wt/vol), a dose 6 times the typically recommended dose for 8 months, which is standard at our institution. With rush desensitization protocols using 0.5 mL of 1:100 wt/vol as maintenance, there is a 98.2% efficacy on day 22 as determined by sting challenges.<sup>4</sup> High maintenance doses have been recommended by the current practice parameters if necessary.<sup>4</sup>

Despite the patient being on immunotherapy for an adequate duration and at a higher dosage, she still had anaphylaxis from an IFA field sting (significant albeit subjective) as well as an injection of IFA WBE immunotherapy. Especially given the documented hypotensive anaphylactic reaction when an attempt was made to restart her on IFA immunotherapy, it was deemed unsafe to continue that modality of treatment. In other circumstances in which there may be an IFA reaction (whether to a field or intentional sting) without a reaction to the WBE immunotherapy itself, the IFA WBE immunotherapy dose would merely be increased; however, this was not prudent given our unique case of a reaction to the WBE immunotherapy itself. Whether a very high dose of WBE immunotherapy (eg, 1.0 mL 1:10 wt/vol) would have been effective is unknown. Furthermore, the patient was frightened to continue immunotherapy. Given the apparent failure of IFA immunotherapy on the basis of safety and efficacy, other theoretically attractive alternatives were explored. Therefore, a therapeutic trial with omalizumab seemed reasonable on the basis of a risk-benefit analysis.

Anti-IgE therapy has been studied in food anaphylaxis (another IgE-mediated anaphylactic reaction) and increased the tolerance to peanut in some individuals with peanut-induced anaphylaxis.<sup>6</sup> Other case reports suggest efficacy of omalizumab for idiopathic anaphylaxis.<sup>7</sup> Omalizumab has also been shown to be effective as pretreatment in individuals with ragweed-allergic rhinitis about to

undergo rush immunotherapy by decreasing their risk of anaphylaxis secondary to immunotherapy 5-fold. It also made the immunotherapy more effective because the patients who received both treatments had less severe symptoms during the ragweed season.<sup>8</sup> In another study, omalizumab was administered with specific immunotherapy, and it significantly reduced the symptom load in patients with seasonal allergic rhinoconjunctivitis and seasonal allergic asthma versus those who received only immunotherapy.<sup>9</sup> The primary mechanism of action of anti-IgE therapy is predicted to be the reduction in serum levels of IgE and FcεRI expression on mast cells and basophils.<sup>7</sup> In targeting IgE, it represents a novel and promising potential approach to a variety of IgE-mediated anaphylactic disorders.

Our case illustrates a patient who underwent unsuccessful attempted treatment with IFA immunotherapy from both a safety and efficacy perspective but responded well to omalizumab. To our knowledge, this is the first report of efficacy of anti-IgE as monotherapy in the treatment of insect sting anaphylaxis specifically. Further controlled studies should be undertaken to explore the efficacy of anti-IgE in insect sting anaphylaxis either as the sole treatment or in conjunction with immunotherapy, and in particular, in those rare patients who fail to respond to the current standard of care for *Hymenoptera* immunotherapy.

Hana M. Tartibi, MD<sup>a</sup>

Amee R. Majmundar, MD<sup>b</sup>

David A. Khan, MD<sup>c</sup>

From <sup>a</sup>the Department of Internal Medicine, Parkland Health and Hospital System, Dallas, Tex; <sup>b</sup>Advanced Allergy and Asthma Care SC, Orland Park, Ill; and <sup>c</sup>the Division of Allergy and Immunology, Department of Internal Medicine, University

of Texas Southwestern Medical Center, Dallas, Tex. E-mail: [Dave.Khan@UTSouthwestern.edu](mailto:Dave.Khan@UTSouthwestern.edu).

Supported by the Division of Allergy and Immunology, University of Texas Southwestern Medical Center.

Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

## REFERENCES

- Freeman TM. Fire ants and killer bees. *Ann Allergy Asthma Immunol* 1997;78:369-72.
- Freeman TM, Hylander R, Ortiz A, Martin ME, et al. Imported fire ant immunotherapy: effectiveness of whole body extracts. *J Allergy Clin Immunol* 1992;90:210-5.
- Tankersley MS, Walker RL, Butler WK, Hagan LL, Napoli DC, Freeman TM. Safety and efficacy of an imported fire ant rush immunotherapy protocol with and without prophylactic treatment. *J Allergy Clin Immunol* 2002;109:556-62.
- Moffitt JE, Golden DB, Reisman RE, Lee R, Nicklas R, Freeman T, et al. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol* 2004;114:869-86.
- Hoffman DR, Jacobson RS, Schmidt M, Smith AM. Allergens in Hymenoptera venoms, XXIII: venom content of imported fire ant whole body extracts. *Ann Allergy* 1991;66:29-31.
- Leung DY, Sampson HA, Yunginger JW, Burks AW Jr, Schneider LC, Wortel CH, et al. Effect of anti-IgE therapy in patients with peanut allergy. *N Engl J Med* 2003;348:986-93.
- Jones JD, Marney SR Jr, Fahrenholz JM. Idiopathic anaphylaxis successfully treated with omalizumab. *Ann Allergy Asthma Immunol* 2008;101:550-1.
- Casale T, Busse W, Kline J, Ballas Z, Moss MH, Townley RG, et al. Omalizumab pretreatment decreases acute reactions after rush immunotherapy for ragweed-induced seasonal allergic rhinitis. *J Allergy Clin Immunol* 2006;117:134-40.
- Kopp M, Hamelmann E, Zielenz S, Kamin W, Bergmann KC, Sieder C, et al. Combination of omalizumab and specific immunotherapy is superior to immunotherapy in patients with seasonal allergic rhinoconjunctivitis and co-morbid seasonal allergic asthma. *Clin Exp Allergy* 2009;39:271-9.

doi:10.1016/j.jaci.2010.06.014