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References

1. Zazzali JL, Kaplan A, Maurer M, et al. Angioedema in the omalizumab chronic idiopathic/spontaneous urticaria pivotal studies. *Ann Allergy Asthma Immunol*. 2016;117:370–377.
2. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria: a GA(2)LEN task force report. *Allergy*. 2011;66:317–330.
3. Zuberbier T, Aberer W, Asero R, Abdul Latiff AH, et al. The EAACI/GA(2)LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy*. 2018;73:1393–1414.
4. Brzoza Z, Badura-Brzoza K, Mlynec A, et al. Adaptation and initial results of the Polish version of the GA(2)LEN chronic urticaria quality of life questionnaire (CU-Q(2)ol). *J Dermatol Sci*. 2011;62:36–41.
5. Ye YM, Park JW, Kim SH, et al. Clinical evaluation of the computerized chronic urticaria-specific quality of life questionnaire in Korean patients with chronic urticaria. *Clin Exp Dermatol*. 2012;37:722–728.
6. Engin B, Uguz F, Yilmaz E, Ozdemir M, Mevlitoglu I. The levels of depression, anxiety and quality of life in patients with chronic idiopathic urticaria. *J Eur Acad Dermatol Venereol*. 2008;22:36–40.
7. Brzoza Z, Kasperska-Zajac A, Badura-Brzoza K, Matysiakiewicz J, Hese RT, Rogala B. Decline in dehydroepiandrosterone sulfate observed in chronic urticaria is associated with psychological distress. *Psychosom Med*. 2008;70:723–728.
8. Ozkan M, Oflaz SB, Kocaman N, et al. Psychiatric morbidity and quality of life in patients with chronic idiopathic urticaria. *Ann Allergy Asthma Immunol*. 2007;99:29–33.
9. Fouche AS, Saunders EF, Craig T. Depression and anxiety in patients with hereditary angioedema. *Ann Allergy Asthma Immunol*. 2014;112:371–375.
10. Choi WS, Lim ES, Ban GY, et al. Disease-specific impairment of the quality of life in adult patients with chronic spontaneous urticaria. *Korean J Intern Med*. 2018;33:185–192.

Imported fire ant hypersensitivity and mastocytosis A case series of successful venom immunotherapy



The prevalence of flying Hymenoptera venom hypersensitivity in patients with mast cell activation disorders (MCADs) is approximately 25% vs 2% in the general population.¹ Previous studies have reported success with venom immunotherapy (VIT) for flying Hymenoptera hypersensitivity in the setting of MCADa.² To date, there are no cases of hypersensitivity to the imported fire ant (IFA), *Solenopsis invicta/Solenopsis richteri* specifically, in patients with MCADa in the literature. Moreover, this case series is the first, to our knowledge, to describe patients with MCADs and documented IFA hypersensitivity who have successfully completed the build-up phase of IFA-whole body extract (WBE) immunotherapy using conventional and rush protocols.

A 39-year-old man presented to the allergy clinic with a 2-episode history of anaphylactic shock with accompanying grand mal seizure after multiple stings from IFAs. Both episodes occurred within 5 to 10 minutes after the stings and resulted in hospitalization with a full neurology workup. A neurologic cause could not be found in either instance. The patient's history was significant for near-daily presyncopal episodes with an unknown trigger. Laboratory evaluation revealed a baseline tryptase level of 25 µg/L and a specific IgE level for IFAs greater than 100 kU/L. The patient was given an epinephrine autoinjector and prescribed daily montelukast, cetirizine, and ranitidine, resulting in resolution of his presyncopal episodes. He was then evaluated for MCADs and found to have hypocellular bone marrow with aberrant CD25⁺ mast cells (MCs) and negative D816V. To verify the diagnosis, subsequent bone marrow biopsy performed 1 year later revealed increased focal aggregates of CD25⁺ MCs and more than 25% CD117⁺/CD2⁺ spindle-shaped MCs.

The patient was diagnosed with indolent systemic mastocytosis based on fulfilling 1 major and 3 minor criteria for systemic mastocytosis.³ He was prescribed a conventional buildup schedule of IFA-WBE VIT as determined by his primary allergist. He completed the build-up phase successfully and achieved monthly maintenance dosing with 0.5 mL of 1:200 wt/vol *Solenopsis invicta/Solenopsis richteri* WBE (Hollister-Stier, Spokane, Washington).

A 52-year-old man presented to the allergy clinic with a history of multiple episodes of anaphylaxis to tomatoes and tomato products and a history of anaphylaxis with shock after multiple stings by IFAs. The episodes of anaphylaxis to tomatoes and IFA

Table 1

One-Day Rush Protocol for Imported Fire Ants

Dose, mL	Concentration (vol/vol)	Observation time, min
0.3	1:1000	30
0.1	1:100	30
0.3	1:100	30
0.05	1:10	30
0.15	1:10	30
0.3	1:10	30
0.05	1:1	30
0.1	1:1	30
0.2	1:1	30
0.3	1:1	60

occurred within 5 to 30 minutes after ingestion (the inciting event). Further evaluation revealed a baseline tryptase level of 18.2 µg/L and specific IgE levels for IFAs and tomato of 1.97 kU/L and 8.45 kU/L, respectively. On follow-up, he reported having periodic flushing episodes without a known trigger as well as intermittent abdominal pain. The patient was given an epinephrine autoinjector and prescribed cetirizine, ranitidine, and cromolyn daily, resulting in resolution of his flushing and abdominal pain. On the basis of a history of severe anaphylaxis to IFAs and tomato, the decision was made to evaluate for an underlying MCAD. A bone marrow biopsy revealed more than 25% spindling of CD2⁺/CD25⁺/CD117⁺ MCs and negative D816V. Although the patient's baseline tryptase level was elevated, laboratory evidence of acute histamine release was unavailable. A diagnosis of MC activation syndrome was made based on recurrent episodic symptoms, response to therapy, and elevated tryptase level.³

Because the patient lives in an IFA endemic area, an accelerated VIT protocol was considered. Literature review reveals that rush immunotherapy (RIT) is efficacious and carries a low systemic reaction rate.^{4–6} The patient was prescribed a previously published protocol that used pretreatment starting 2 days before the desensitization with cetirizine, ranitidine, and prednisone.⁶ The protocol consisted of 10 steps of incremental dose and concentration increases of *Solenopsis invicta/Solenopsis richteri* WBE (Hollister-Stier) (Table 1). This treatment was then followed by a maintenance dose of 0.5 mL of a 1:200 wt/vol *Solenopsis invicta/Solenopsis richteri* WBE (Hollister-Stier) on days 8, 15, 29, and 50.⁶ The patient tolerated the rush protocol well and continues to receive monthly maintenance dosing and daily therapy with

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cetirizine, ranitidine, and cromolyn without further anaphylaxis episodes.

This case series demonstrates IFA hypersensitivity in patients with MCADs. It also provides examples of successful IFA-WBE desensitization using conventional and rush protocols.

In adults with insect allergy, the prevalence of mastocytosis is approximately 2%, whereas the prevalence of monoclonal MC activation syndrome and nonclonal MCAD is unknown.⁷ The occurrence of anaphylaxis attributable to insect stings in patients with mastocytosis is approximately 25%, highlighting an increased risk of systemic reactions to venom.¹ Through extrapolation from flying Hymenoptera data, it can be argued that patients with MCADs are at increased risk of anaphylaxis to IFA stings, particularly given that IFAs are the most frequent cause of insect venom hypersensitivity in the Southeast United States.^{7,8} Thus, depending on the severity of reaction to IFAs, we recommend obtaining a baseline tryptase measurement to screen for MCAD. If elevated, confirmation of underlying pathologic findings is warranted as demonstrated by our case series. A need to manage IFA venom hypersensitivity also exists in patients with MCADs, especially those living in endemic regions.⁹

Multiple studies have confirmed the efficacy and safety of flying Hymenoptera VIT in patients with mastocytosis.^{2,10} The safety and efficacy of IFA-WBE VIT in the setting of MCAD can be extrapolated from these data. Furthermore, studies have established the safety and efficacy of RIT and conventional VIT in patients treated for IFA hypersensitivity.^{4,6} We present these modes of IFA-WBE VIT in 2 patients with MCADs. Adherence to VIT continues to be a significant problem because of logistical difficulties.⁶ RIT is an efficacious, safe, and convenient therapy for IFA-WBE allergic patients.⁶

We argue that RIT should be strongly considered for every patient with an MCAD who has documented IFA hypersensitivity.¹⁰ Given the increased risk of reaction in patients with MCADs, we recommend premedication of patients with MCADs before RIT.⁶ RIT is a viable option when the risk of additional stings and the degree of severity of the initial reaction is high.

This case series provides examples of successful IFA-WBE desensitization using conventional and rush protocols in patients with MCADs. The effective and efficient management of IFA venom hypersensitivity in patients with MCADs is paramount. Thus, RIT for IFA-WBE should be strongly considered for patients with MCADs.

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References

1. Niedoszytko M, Bonadonna P, Oude-Elberink JNG, Golden DBK. Epidemiology, diagnosis, and treatment of Hymenoptera venom in allergy in mastocytosis patients. *Immunol Allergy Clin North Am*. 2014;34:365–381.
2. Gonzalez de Olano D, Alvarez-Twose I, Esteban-Lopez M, et al. Safety and effectiveness of immunotherapy in patients with indolent systemic mastocytosis presenting with Hymenoptera venom anaphylaxis. *J Allergy Clin Immunol*. 2008;121:519–526.
3. Akin C, Valent P, Metcalfe D. Mast cell activation syndrome: proposed diagnostic criteria. *J Allergy Clin Immunol*. 2010;126:1099–1104.
4. Judd CA, Parker AL, Meier EA, et al. Successful administration of a 1-day imported fire ant rush immunotherapy protocol. *Ann Allergy Asthma Immunol*. 2008;101:311–315.
5. Tankersley MS, Walker RL, Butler WK, et al. Safety and efficacy of an imported fire ant rush immunotherapy protocol with and without prophylactic treatment. *J Allergy Clin Immunol*. 2002;109:556–562.
6. Arseneau AM, Nesselroad TD, Dietrich JJ, et al. A 1-day imported fire ant rush immunotherapy schedule with and without premedication. *Ann Allergy Asthma Immunol*. 2013;111:562–566.
7. Golden DB, Demain J, Freeman T, et al. Stinging insect hypersensitivity: a practice parameter update 2016. *Ann Allergy Asthma Immunol*. 2017;118:28–54.
8. Asawa A, Simpson KH, Bonds RS. Ketotifen use in a patient with fire ant hypersensitivity and mast cell activation syndrome. *Ann Allergy Asthma Immunol*. 2015;114:443–446.
9. Akin C. Mast cell activation disorders. *J Allergy Clin Immunol Pract*. 2014;2:252–257.
10. Bonadonna P, Zanotti R, Caruso B, et al. Allergen specific immunotherapy is safe and effective in patients with systemic mastocytosis and Hymenoptera allergy. *J Allergy Clin Immunol*. 2008;121:256–257.