



Letter

Delayed stinging insect reactions

Systemic allergic reactions to stinging insects occur in approximately 1% of children and 3% of adults.¹ Immunoglobulin E (IgE)-mediated reactions can present as systemic reactions or large local reactions.¹ Systemic reactions present with symptoms related to urticaria, angioedema, airway obstruction, and hypotension (and sometimes abdominal pain, bronchospasm, or cardiac abnormalities) within 5 to 30 minutes after an insect sting.² Large local reactions present as swelling of at least 10 cm in diameter that is contiguous with the sting site, increases in size for 1 to 2 days, and resolves over 5 to 10 days.¹ Venom immunotherapy (VIT) is the standard of care in adults with a history of systemic reactions.¹ However, large local reactions carry a low risk of a future systemic reaction and generally do not require VIT.¹

Although rarely described in the literature, insect sting reactions can have a delayed onset in contrast to the typical IgE-mediated reaction. We describe the case of a patient who developed an immediate large local reaction, and then a delayed systemic urticarial reaction, after an insect sting.

A 59-year-old woman was evaluated after being stung and developing an atypical reaction. She was stung while gardening during the day and noted an insect fly out of a log in the garden that stung her. She developed swelling in the area of the sting that increased in size over the course of approximately 1 day. There was no associated urticaria, respiratory, circulatory, or gastrointestinal symptoms. The localized swelling resolved within approximately 1 week. Two weeks after the initial reaction, she developed a recurrence of extensive localized swelling in the area of the sting associated with generalized urticaria (pruritic, erythematous, raised) and a subjective sensation of mouth swelling. The reaction was not associated with arthralgias, joint swelling, fever, urinary changes, or other systemic symptoms. The overall reaction lasted several days and resolved with no residual bruising or pigmentary changes to the skin. She could not identify which insect had stung her.

Her medical history was notable for dermatographism that was well controlled with a daily or twice-daily second-generation antihistamine. At the time of the initial and delayed reaction, she was on a once-daily second-generation antihistamine. In addition, the patient had a history of persistent rhinitis symptoms. There was no history of asthma or atopic dermatitis. Review of systems and a complete physical examination were unremarkable, other than edematous and pale nasal mucous membranes.

The patient underwent intradermal testing to the stinging insects, the result of which was positive to yellow jacket and yellow hornet (tested at 1 μ g/mL) and negative to white-faced hornet, paper wasp, and honeybee. Saline control showed negative results. Tryptase was normal (<3 μ g/L). Serum specific IgE was positive to yellow jacket (1.4 kU/L) and paper wasp (0.5 kU/L) and

undetectable (<0.35 kU/L) to honeybee, white-faced hornet, and yellow hornet. Epicutaneous testing to seasonal and perennial aeroallergens showed positivity to dust mite.

The patient was started on yellow jacket immunotherapy. She underwent immunotherapy to yellow jacket in isolation because it was the only stinging insect showing positive results for intradermal testing and serum specific IgE and is the most common cause of stinging insect reactions in Canada. She has been tolerating it well. She has since been stung once while walking outside by an unknown insect with no reaction.

Delayed anaphylactic reactions have been reported in the literature. A prospective analysis of 412 anaphylactic reactions reported a delayed deterioration in 9.2% of cases.³ However, they are rarely reported to occur with venom stings. A literature search of PubMed yielded 3 previous reports of such types of reactions. A case series published in 1989 included 10 patients with late-onset allergic reactions 7 to 14 days after the initial sting.² A case report described recurrent anaphylaxis in a man who developed delayed anaphylactic reactions (hours to a few days later).⁴ A case series of 15 patients with unusual reactions after insect stings described 1 patient who had 2 delayed reactions to insect stings: one was delayed angioedema that recurred within 6 hours and the other was localized swelling followed by an anaphylactic reaction 10 hours later.⁵ In addition, a large national registry of patients with insect allergy who had testing and treatment reported many individuals who stated the onset of systemic reaction was hours after the sting.⁶ However, none of the cases of delayed insect stings described in the literature, to our knowledge, consist of an initial large local reaction followed by a delayed systemic urticarial reaction.

The delayed reaction could have been a flare of her dermatographism, although this was deemed less likely because it had been stable for an extended period, she was on a daily antihistamine, and the systemic urticarial reaction coincided with repeat acute onset of angioedema in the area of the sting. Delayed non-IgE-mediated reactions to insect stings have been described in the literature, including serum sickness, renal disease, and cold contact urticaria.^{5,7} Although serum sickness does present with delayed urticaria, serum sickness was judged unlikely in our case because of the absence of other systemic symptoms. However, our conclusion that this was a delayed IgE-mediated reaction would have been further strengthened with a sting challenge.

The pathophysiology leading to delayed-onset IgE-mediated reactions is unknown. Reisman and Livingston,² in their case series, postulated that this reaction occurs from stimulation of IgE production, which reacts with venom antigen that has persisted in the system until the reaction. Should this be the case, then the patient would be at risk of a future systemic reaction with another sting, and as a result immunotherapy could be recommended. Previous reports of delayed reactions have described patients who often

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elected to proceed with VIT, which successfully prevented future systemic reactions.^{2,4}

In conclusion, this case is unique because it presents the first known reported immediate large local reaction followed by a systemic urticarial reaction with recurrence of the large local reaction. It demonstrates that delayed-onset systemic reactions can occur up to 2 weeks after the culprit sting.

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Elissa M. Abrams, MD
Allan B. Becker, MD
Department of Pediatrics
Section of Allergy and Clinical Immunology
University of Manitoba
Winnipeg

Manitoba, Canada
elissa.abrams@gmail.com

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