
Natural history of large local and generalized cutaneous reactions to imported fire ant stings in children

Steven A. Nguyen, MD, and Diane C. Napoli, MD

Background: There are no published data on the natural history of large local and generalized cutaneous reactions to imported fire ant (IFA) stings in children.

Objective: To determine the natural history of large local and generalized cutaneous reactions to IFA stings in children not treated with immunotherapy by reviewing medical records from a venom clinic during the past 20 years.

Methods: Patients were selected for the study if they were 16 years or younger at the time of the reaction, had only cutaneous symptoms (generalized cutaneous or large local), and did not initiate immunotherapy. Each patient's parents were asked to recall whether the patient had experienced any further stings since the last evaluation at the venom clinic.

Results: We contacted 31 of 57 patients evaluated between July 10, 1984, and February 5, 2004. Twenty patients (65%) reported that they had not developed more severe reactions with subsequent stings. Reactions remained cutaneous only. Eleven patients (35%) had not been stung again since the original evaluation. Five of these patients had moved out of the IFA-endemic region. None of the previously evaluated patients reported subsequent life-threatening anaphylaxis from IFA stings.

Conclusions: These limited data on IFA stings suggest a benign outcome in children 16 years and younger with large local or generalized cutaneous reactions. Larger and more extensive studies need to be conducted to further define the natural history of cutaneous reactions to IFA stings in children.

Ann Allergy Asthma Immunol. 2005;94:387-390.

INTRODUCTION

Imported fire ants (IFAs) from South America infest large areas of the southern United States, with penetration into Puerto Rico, Arizona, New Mexico, and California.¹ *Solenopsis invicta*, the red IFA and the most aggressive species, has almost completely eradicated native ant species, including the southern fire ant, *Solenopsis xyloni*, as well as the tropical fire ant, *Solenopsis geminata*, and the black IFA, *Solenopsis richteri*.² Current evidence indicates that through interbreeding with local ant species, their range is expanding because new hybrids display drought and cold resistance.³ Recently, IFA colonies and cases of anaphylaxis have been reported as far as Brisbane, Australia.⁴ As the geographic range of the IFA expands, its medical significance will increase. Consequently, it is critical to be able to predict a patient's risk for anaphylaxis with subsequent stings.

Allergic reactions to IFA stings can present as local inflammation of various sizes, generalized cutaneous symptoms with urticaria and angioedema, or severe systemic, life-threatening reactions. The current stinging insect hypersensitivity practice parameter⁵ criteria for starting immunotherapy for a life-threatening systemic reaction are the same

for IFAs and flying Hymenoptera (ie, a history of systemic reactions and demonstration of IFA antigen specific IgE antibodies by skin or in vitro testing). Current management of large local reactions (LLRs) and generalized cutaneous reactions for children 16 years and younger after a flying Hymenoptera sting consists of avoidance measures and no immunotherapy. This practice is based on prospective studies⁶ that reported a 10% risk of systemic reaction with future stings. However, the management of children 16 years and younger who have systemic reactions that are confined to the skin from an IFA sting is controversial, because there has been no study demonstrating the relative risk of a systemic reaction after subsequent stings. Traditional management of these cutaneous reactions without any other systemic symptoms consists of education on avoidance measures and usually no immunotherapy. This recommendation is based primarily on extrapolation from the literature on cutaneous-only reactions to flying Hymenoptera stings in children.⁶ However, unlike the treatment of cutaneous reactions to flying Hymenoptera, up to 29% of allergists initiate IFA whole-body extract immunotherapy in these children because of frequent or unavoidable future stings in fire ant-endemic areas.⁷ Thus, the parameter⁵ states that immunotherapy in these children is considered to be optional at the present time. A MEDLINE search (1950 to 2004) on the natural history of cutaneous-only reactions to IFA stings in children did not identify any published data on this subject. There also are no published data on the natural history of LLRs to IFA stings in children. We sought to determine the natural history of untreated large

Allergy/Immunology, Wilford Hall Medical Center, San Antonio, Texas. The opinions and assertions contained herein are the private views of the authors and are not to be construed as reflecting the views of the Department of the Air Force, the Department of Defense, or the United States government.

Received for publication April 23, 2004.

Accepted for publication in revised form August 1, 2004.

local and generalized cutaneous reactions to IFA stings in children who had been seen in the venom clinic at Wilford Hall Medical Center, Lackland AFB, San Antonio, TX, during the past 20 years.

METHODS

Participants

A venom logbook containing information from patients previously evaluated for fire ant stings has been maintained since 1984. Patients were selected for the study if they were 16 years or younger at the time of their sting, had only cutaneous symptoms (generalized cutaneous or large local), and were not given immunotherapy. To compare the data from this study with those from Valentine et al⁶ on the value of immunotherapy with venom in children with allergy to flying Hymenoptera, a cutoff age of 16 years was chosen. Patients with signs or symptoms suggestive of more severe reactions, such as hoarseness, dyspnea, wheezing, or lightheadedness (implying respiratory or cardiovascular involvement), were excluded from the study.

Interview

After approval from the institutional review board at Wilford Hall Medical Center, attempts were made to locate all eligible patients by telephone or e-mail. The patient's parents were interviewed, and they were asked to recall whether the patient had experienced any further stings since the last evaluation at the venom clinic. They were asked to describe any reactions in detail, focusing on signs and symptoms of further systemic reaction development. If they did not know the answer, they could ask the patient or other caretaker to provide further input.

RESULTS

Fifty-seven patients evaluated between July 10, 1984, and February 5, 2004, met the study criteria. The Allergy/Immunology Department at Wilford Hall Medical Center in southern Texas primarily serves a mobile, transient military population. Consequently, some of these patients had since relocated to other areas of the United States or the world and were no longer living in fire ant-endemic areas. Fifteen patients who were evaluated before 1991 could not be found owing to insufficient documentation of patient locator information (incomplete Social Security number, name, address, telephone number, etc). Their medical records were not available for review.

Between February 27, 1991, and February 5, 2004, we evaluated 864 patients for insect sting reactions; 43% of these patients had IFA sting reactions (11% were children ≤ 16 years and 32% were adults). The IFA sting reaction group was further divided into large local, generalized cutaneous, and systemic reactions (Table 1). In children who were evaluated for an IFA sting reaction, 18% had large local, 23% had generalized cutaneous, and 59% had systemic reactions. The adult IFA sting reaction group presented less often with large

Table 1. Imported Fire Ant Presentations in 378 Patients: 1991–2004

Presentation	Patients, No. (%)	
	Children ≤ 16 y (n = 99)	Adults (n = 279)
Large local	18 (18)	41 (15)
Generalized cutaneous	23 (23)	35 (13)
Systemic	58 (59)	203 (73)

local (15%) and generalized cutaneous (13%) reactions and more often with systemic reactions (73%) overall.

We contacted 31 patients (16 boys and 15 girls) who met the inclusion criteria (12 with large local and 19 with generalized cutaneous reactions). We could not locate 12 other patients who also met the inclusion criteria but had incorrect forwarding addresses and telephone numbers. No family refused to provide information when surveyed. The mean age at the time of the initial evaluation was 6.2 years (range, 1.5–16.0 years). The mean time since the original evaluation was 4.9 years (range, 0.25–11.5 years).

Of the 31 patients contacted, none of the 20 (65%) who were stung again developed more severe reactions with subsequent stings. Twelve of these patients originally presented with generalized cutaneous reactions, and 8 had LLRs. Most patients developed small to large local reactions at the sting sites. The remaining 11 patients (35%) had not been stung again since the original evaluation: 7 originally presented with generalized cutaneous reactions and 4 with LLRs. Five of these patients without repeated stings had moved out of the fire ant-endemic region. None of the patients previously evaluated for large local and generalized cutaneous reactions reported subsequent life-threatening anaphylaxis from IFA stings. A few patients were given antihistamines at the onset of swelling, but none required epinephrine therapy.

The family and patient histories of atopy were not obtained at the time of the survey. Serum IgE and IgG samples were not collected from any of the children with large local or generalized cutaneous skin reactions. Three patients with generalized cutaneous reactions and an additional history of questionable further systemic development (noisy breathing, nausea, and facial angioedema, respectively) were skin tested with IFA whole-body extract. Patient 1, with the additional symptom of noisy breathing, had negative test results and continued having local reactions to subsequent stings. Patient 2, who also reported additional nausea, tested positive at 1:100,000 intradermal and was offered immunotherapy. Her parent declined immunotherapy, and she was given injectable epinephrine and was advised on avoidance measures. She continued having LLRs with subsequent stings. Patient 3, with facial angioedema, had a 4+ skin prick test reaction to IFA stings. Her parent also declined immunotherapy, and she was given injectable epinephrine. The patient still lives in an IFA-endemic area, but she has not been stung again in 3 years by practicing avoidance measures.

DISCUSSION

Tracy et al⁸ studied 107 patients who were not sensitized to IFA stings in an endemic area and reported a sting attack rate of 51% during a 3-week period. A study by Freeman⁹ in this same endemic area showed that reactions to IFA stings were responsible for 42% of the visits in a venom clinic during a 10-year period. deShazo et al¹⁰ reported that of patients who had been stung by IFAs, 17% to 56% developed LLRs. Life-threatening anaphylaxis, however, occurs infrequently. In a 1989 survey,¹¹ physicians in 13 southern states were queried to evaluate the magnitude of medical problems caused by IFA stings. Of the 29,205 physicians surveyed, 2,022 (7%) reported treating approximately 20,755 patients annually for IFA sting reactions, but only 2% required treatment for life-threatening anaphylaxis.¹¹

Despite the low prevalence of life-threatening reactions, at least 44 deaths due to IFA stings have been reported in the medical literature during the past half century.¹² Because of fear of the potential for more severe life-threatening future reactions, at least 29% of allergists in a 1997 survey still recommended immunotherapy for generalized cutaneous reactions,⁷ despite the lack of data to support or refute this practice.

Previous studies addressing the natural history of allergy to Hymenoptera stings have been reported only for flying Hymenoptera. Abrecht et al¹³ reported that the likelihood of a subsequent sting resulting in a systemic reaction in a patient with a history of severe local reactions to flying Hymenoptera was 33% (59/177). Of these systemic reactions, 15% were life-threatening. Thus, the probability of experiencing a life-threatening reaction with a subsequent sting after a severe local reaction is approximately 5%. Golden et al¹⁴ surveyed 103 patients with previous LLRs to flying Hymenoptera; 52 had interim stings that caused 5 systemic reactions (10%) and 39 LLRs (75%). Graft et al¹⁵ reported that only 2 (2%) of 113 stings in children with previous LLRs resulted in systemic reactions. One of these systemic reactions was a potentially life-threatening reaction (mild-to-moderate laryngeal edema). The degree of allergic sensitivity measured by venom skin tests or specific IgE antibody levels that existed before subsequent stings was not predictive of sting outcome.

A similar conclusion was presented by Mauriello et al¹⁶ in their review of 133 patients (age range, 2–80 years) with LLRs to flying Hymenoptera. They collected serum samples from these patients for analysis of venom specific IgE and performed intradermal testing with various insect venoms. After dividing the patients into radioallergosorbent test (RAST)-positive and RAST-negative groups, they followed them for a mean of 3 years to evaluate the subsequent sting experience. Of the 66 patients who were RAST negative, 58% had positive skin test reactions to 1 or more venoms. Seventy-five subsequent stings in this group led to no systemic reactions and 74 LLRs. Results of RASTs remained negative, and the incidence of positive skin test reactions was unchanged at follow-up. Twenty-four of 67 RAST-positive

patients received immunotherapy. Fifty-five subsequent stings were reported in this RAST-positive group, with 40 recurrent LLRs occurring equally in treated and untreated patients. Although 1 systemic reaction (4%) occurred in 24 subsequent sting cases in untreated RAST-positive patients, the rest continued to have LLRs. Thus, they concluded that identifying serum venom specific IgE in patients with LLRs to flying Hymenoptera stings did not aid in treatment or in predicting prognosis.

In a study¹⁷ of 235 children with a history of allergic reactions to flying Hymenoptera, 68% (123/182) of the patients with a history of systemic reactions reported only cutaneous symptoms. During the first year of a study in a generalized cutaneous reaction group without immunotherapy, Schuberth et al¹⁷ reported that 20 accidental stings produced 2 mild systemic reactions and 4 LLRs, all of which resolved without the use of epinephrine. In no case was the subsequent systemic reaction as serious as the original.

A follow-up study by Valentine et al⁶ that evaluated the value of immunotherapy with venom in children with generalized cutaneous reactions showed similar results. In the treated group, 84 stings in 36 patients resulted in 1 systemic reaction (1.2% of stings), whereas 196 stings in 86 untreated children resulted in 18 systemic reactions (9.2% of stings). These reactions were milder than or similar to the first sting reactions, and none were more severe.

We sought to determine the natural history of large local and generalized cutaneous reactions to IFA stings in children who were not treated with immunotherapy by reviewing medical records from a venom clinic during the past 20 years. Our limited data on IFA stings suggest a benign outcome in children 16 years and younger with cutaneous-only reactions. These findings are consistent with existing flying Hymenoptera literature that suggests that immunotherapy is unnecessary for these children. However, specific treatment recommendations cannot be concluded from these small numbers. Larger and more extensive studies need to be conducted to further define the natural history of cutaneous reactions to IFA stings in children.

REFERENCES

1. Kemp SF, deShazo RD, Moffitt JE, et al. Expanding habitat of the imported fire ant (*Solenopsis invicta*): a public health concern. *J Allergy Clin Immunol*. 2000;105:683–691.
2. Rhoades RB. Fire ant allergy: diagnosis and treatment. *Immunol Allergy Pract*. 1987;9:23–31.
3. Vander Meer RK, Lofgren CS. Biochemical evidence for hybridization in fire ants. *Fla Entomol*. 1985;68:501–506.
4. Solley GO, Vanderwoude C. Fire ant sting anaphylaxis in Australia [abstract]. *J Allergy Clin Immunol*. 2004;113:S75.
5. Portnoy JM, Moffitt JE, Golden DBK, et al. Stinging insect hypersensitivity: a practice parameter. *J Allergy Clin Immunol*. 1999;103:963–980.
6. Valentine MD, Schuberth KC, Kagey-Sabotka A, et al. The value of immunotherapy with venom in children with allergy to insect stings. *N Engl J Med*. 1990;323:1601–1603.
7. Moffitt JE, Barker JR, Stafford CT. Management of imported

-
- fire ant allergy: results of a survey. *Ann Allergy Asthma Immunol.* 1997;79:125–130.
8. Tracy JM, Demain JG, Quinn JM, et al. The natural history of exposure to the imported fire ant (*Solenopsis invicta*). *J Allergy Clin Immunol.* 1995;95:824–828.
9. Freeman TM. Hymenoptera hypersensitivity in an imported fire ant endemic area. *Ann Allergy Asthma Immunol.* 1997;78:369–372.
10. deShazo RD, Griffing C, Kwan TH, et al. Dermal hypersensitivity reactions to imported fire ants. *J Allergy Clin Immunol.* 1984;74:841–847.
11. Stafford CT, Hutto LS, Rhoades RB, et al. Imported fire ant as a health hazard. *South Med J.* 1989;82:1515–1519.
12. Prahlow JA, Barnard JJ. Fatal anaphylaxis due to fire ant stings. *Am J Forensic Med Pathol.* 1998;19:137–142.
13. Abrecht I, Eichler G, Muller U, Hoigne R. On the significance of severe local reactions to Hymenoptera stings. *Clin Allergy.* 1980;10:675–682.
14. Golden DBK, Johnson K, Addison BI, et al. Evolution of Hymenoptera venom allergy [abstract]. *J Allergy Clin Immunol.* 1984;73:S189.
15. Graft D, Schuberth K, Kagey-Sobotka A, et al. A prospective study of the natural history of large local reactions after Hymenoptera stings in children. *J Pediatr.* 1984;104:664–668.
16. Mauriello PM, Barde SH, Georgitis JW, Reisman RE. Natural history of large local reactions from stinging insects. *J Allergy Clin Immunol.* 1984;74:494–498.
17. Schuberth K, Lichtenstein LM, Kagey-Sobotka A, et al. An epidemiologic study of insect allergy in children, I: characteristics of the disease. *J Pediatr.* 1982;100:546–551.
- Requests for reprints should be addressed to:*
Steven A. Nguyen, MD
4604 Pinehaven Dr
Ocean Springs, MS 39564
E-mail: steven.nguyen@keesler.af.mil
-

Answers to CME examination—Annals of Allergy, Asthma & Immunology, March 2005 Portnoy JM, Kwak K, Dowling P, VanOsdos T, Barnes C. Health effects of indoor fungi. *Ann Allergy Asthma Immunol.* 2005;94:313–320.

1. e
2. b
3. c
4. b
5. e