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Case Report

Anaphylaxis and delayed hymenoptera in a child with fire ant envenomation

Abstract

The red imported fire ant is a species of *Hymenoptera* native to South America, which has spread throughout much of the United States. Hymenoptera envenomations can cause severe allergic reactions and anaphylaxis as well as severe toxin-mediated systemic reactions including rhabdomyolysis, renal failure, liver injury, and coagulopathy. However, red imported fire ant envenomations have rarely been reported to cause these systemic toxin-mediated effects. Here we present the first reported pediatric case of a 2-year-old male infant who presented with both anaphylaxis and evolving signs of systemic envenomation, including rhabdomyolysis and renal failure, as a result of multiple fire ant stings. The case illustrates the potential for a significant hymenoptera toxidrome in the setting of multiple stings and emphasizes the importance of close follow-up given the potential for slowly evolving findings.

The red imported fire ant (*Solenopsis invicta* Buren) is a species of *Hymenoptera* native to South America which was inadvertently introduced to the United States in the 1930s. They have since spread throughout the southeastern and south central United States as well as the west coast and Puerto Rico.[1] Fire ant envenomation is a well-known cause of anaphylaxis in children [2,3] and adults [2,4–8] but has rarely been implicated as a cause of severe systemic reactions beyond those of anaphylaxis, even in the setting of numerous stings.[9,10] Multiple stings by other insects from the order of *Hymenoptera* (including wasps, honeybees, yellow jackets, and hornets) have been shown to induce a specific toxidrome of rhabdomyolysis, renal failure, elevation of liver enzymes, coagulopathy, anemia, and dysfunction in multiple organ systems in both children [11–19] and adults [16,18,20–23]. In addition, single case reports have described nephrotic syndrome[24] and cardiac failure [10] in response to multiple fire ant stings in children. Here we present the case of a 2-year-old male subjected to multiple fire ant stings, who presented with both anaphylaxis and evolving signs of a specific *Hymenoptera* toxidrome. These manifestations, including rhabdomyolysis, coagulopathy, transaminitis, and renal failure, were attributable to direct systemic effects from the venom and evolved over several days. A case of rhabdomyolysis and renal failure following fire ant envenomation has been reported in an adult patient [25], but to date, no case of this specific systemic toxidrome attributable to fire ant stings has been reported in a child.

A 2-year-old African American male was found at a birthday party with ants on both feet. Approximately 10 minutes later, his family noted facial swelling. The child then had emesis once and became unresponsive. Emergency Medical Services was called and arrived within 20 minutes. They described the patient as flaccid and slightly cyanotic. His heart rate was 178 beats per minute (bpm), and his pulse

was described as “weak.” Respiratory rate was 10/minute and “irregular.” The blood pressure was unable to be obtained. Bag-mask ventilation was begun and rhonchi and wheezing were heard on auscultation. Intra-muscular epinephrine was given, and the patient was transported to a local hospital.

In the emergency department (ED) heart rate was 60 bpm and his blood pressure was 124/59 mm Hg. Patient was described as flaccid and therefore electively intubated. Subsequent hypotension (64/28 mm Hg) and tachycardia (160 bpm) was treated with approximately 20 mL/kg intravenous (IV) normal saline (NS) bolus. Laboratory values were remarkable for severe metabolic acidosis (pH 6.8 and lactate 13 mmol/L), elevated white blood cell count (27,000 K/mm³ with 82% neutrophils and 1% bands). Concern over a persistent altered mental status prompted a urine drug screen and a head computed tomography scan, both of which were normal. Patient was transported to The Medical University of South Carolina (MUSC) Children's Hospital Pediatric Intensive Care Unit (PICU). In route to MUSC patient was hypothermic (33.6°C) with a relative tachycardia (144 bpm) and a blood pressure of 87/39 mmHg but displayed poor perfusion and delayed capillary refill and therefore was given an additional 40 mL/kg of IV NS.

Upon admission to the (PICU) vital signs were: temperature 33.8°C; heart rate 144 bpm; blood pressure 96/45 mm Hg; respiratory rate (ventilator) 18/min. On physical exam lips were slightly swollen. Lungs had mild bilateral rhonchi and abdomen was mild to moderately tender to palpation. There was no evidence of ant bites on either foot. Over the next eight hours an additional 60 mL/kg IV NS and continuous dopamine (between 5–8 µg/kg per minute) were needed to maintain cardiovascular stability.

Initial and serial laboratory values are listed in Table 1. Hyperkalemia was corrected with IV sodium bicarbonate and albuterol nebulizations. Hypocalcemia required calcium gluconate and transient hyperglycemia was managed with an insulin drip. Progressive coagulopathy and thrombocytopenia required transfusion of fresh-frozen plasma. Forty-eight hours after admission patient developed rhabdomyolysis with a peak creatine kinase of 370,448 IU/L (normal 25–260 IU/L) and a continuous sodium bicarbonate infusion was initiated. Urine output remained >0.5 mL/kg per hour despite a serum creatinine that peaked at 2.6 mg/dL 72 hours after admission. Transient liver dysfunction with a peak alanine aminotransferase of 1961 IU/L occurred 96 hours after admission. Immunoglobulin E (specific for fire ants) was 28 KU/L (17.5 KU/L is considered very high).

Twelve hours after admission the patient was extubated and weaned off the dopamine drip. Dialysis was not required. On hospital day 7, approximately 30 characteristic pustules were evident on the patient's feet and lower legs. At hospital discharge creatinine was 1.3 mg/dL, creatine kinase was 710 IU/L, and patient was neurologically intact. Junior EpiPen with instructions were prescribed. Follow-up appointments in allergy-immunology and nephrology clinics were

Table 1
Serial laboratory studies through the first week of hospital admission

	Admit	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Na	135	141	144	148	138	136	137
K	7.1	3.6	4.2	4.2	2.7	2.6	3.2
Cl	103	114	116	119	105	100	97
CO ₂	10	15	17	19	23	27	31
BUN	12	21	40	49	46	42	38
Cr	1	1.4	2.3	2.6	2.6	2.6	2.6
WBC	27.3	28.9	16.6	15	16.2	11.8	10.2
Hgb/Hct	12.3/ 37.5	12.3/ 35.9	9.8/28.3	8.6/25.4	8.2/24.1	8.5/25.1	7.9/ 23.6
Platelets	226	164	86	88	93	91	102
INR	1.83	2.35	1.86	1.61	1.14	1.11	N/A
AST/ALT	640/ 312	2703/ 857	4897/ 1563	4460/ 1894	2045/ 1961	1538/ 1466	825/ 1106
CK	N/A	88,598	370,448	105,000	89,841	29,110	12,743
Lactate	13	5.9	0.68	0.6	N/A	N/A	N/A
Glucose	495	251	113	126	176	121	122
PO ₄	15.7	7.4	8.4	7.3	4.2	3.5	3.6
Alb	2.5	2.7	2.3	2.1	1.9	1.9	2
iCa	0.82	1.19	1.03	1.02	1.02	N/A	N/A

Note the development of renal failure, liver injury, coagulopathy, anemia, and worsening rhabdomyolysis over several days.

scheduled. At nephrology follow-up, 1 month after discharge, creatinine was 0.3 mg/dL.

Although reported in other hymenoptera insects, this case represents the first case report of a child stung by fire ants (*S invicta* Buren) presenting with the rare but described syndrome from hymenoptera envenomation. This case report underscores the potential cascade of direct systemic toxic effects of hymenoptera envenomation beyond the more immediate immune-mediated anaphylactic reaction. Although clinicians are aware of acute hypersensitivity reactions secondary to stings from *Hymenoptera* insects, it is less appreciated that multiple stings may uncommonly lead to significant end-organ injury and even mortality. In fact, a clinical and laboratory pattern described by Broides et al [11] as possible in multiple hymenoptera stings manifests as rhabdomyolysis and elevated liver enzymes followed by renal dysfunction and anemia.

This patient's initial facial edema, respiratory distress and unresponsiveness within 10 minutes of fire ant stings and subsequent cardiovascular instability were most likely consistent with anaphylaxis. Allergic hypersensitivity to proteins in *Hymenoptera* venom may lead to large local reactions or systemic reactions typical of immunoglobulin E-mediated type I anaphylactic reactions [26]. In endemic areas fire ants are the most common Hymenoptera species responsible for hypersensitivity reactions [27]. Our patient's elevated fire ant specific IgE revealed prior sensitization to this hymenoptera species – not surprising given the ubiquitous distribution of fire ants in the Southeast. He will undergo specific fire ant immunotherapy by desensitization to lessen the likelihood of a subsequent anaphylactic reaction. Referral for hymenoptera hypersensitivity is supported by practice parameters [28].

Aside from hypersensitivity reactions, fire ants have rarely been implicated in systemic toxicity from direct mass envenomation by multiple bites despite the fact that these insects often attack en masse, and a single ant will commonly sting multiple times. A report by Hardwick et al [10] describes a near fatal presentation of a 5-day-old neonate with shock, coma, hemolysis and coagulopathy following an estimated 2000 stings. However, renal function was not addressed. Myoglobin and creatine kinase were not checked and the patient's electrolytes were described as normal upon presentation.

Although the exact number of stings our patient suffered was not initially apparent, numerous pustules erupted on hospital day 7. The cutaneous manifestations of fire ant stings may not be visible on presentation making the absolute number of bites difficult to determine. Much of the venomous qualities of the fire ant are due to piperidines—toxic alkaloids which have hemolytic, cytotoxic and

even neurotoxic effects [1,29]. Venomous alkaloids are also capable of complement pathway activation. The alkaloid component creates local tissue necrosis and histamine release that manifests as pain and produces the characteristic local sterile pustules. Fire ant venom also contains substantial quantities of formic acid which inhibits cytochrome oxidase activity and has been incriminated as a major factor leading to cell death and rhabdomyolysis [25].

A number of isolated case reports have documented the acute systemic effects of massive envenomation from other stinging hymenoptera insects but few case series have documented a stereotypical progression of delayed features of hymenoptera venom injury. A report from Thailand documented hemolysis and rhabdomyolysis after an unreported number of wasp stings in 7 children referred for acute renal failure [17]. Three of the children had jaundice and elevated transaminases consistent with mild hepatic dysfunction. One patient died of acute renal failure complications but the remaining patients recovered after a period of dialysis. Notably the patients presented 1 to 9 days post stinging episodes. In 2010 Broides et al documented the clinical progression of six children with multiple hymenoptera stings in detail [11]. One patient died by 13 hours after multiple hornet stings with refractory shock and multi-organ failure including rhabdomyolysis, elevated liver enzymes, and metabolic acidosis. The remaining 5 patients, one of whom had only an estimated 6 to 7 yellow jacket stings, followed a remarkably similar pattern that our patient demonstrated. Rhabdomyolysis, hepatic transaminitis, and mild coagulopathy peaked in the first 1 to 3 days followed by gradual renal deterioration peaking at 4 to 9 days post stinging episode. Anemia became apparent by 4 to 13 days. Only one patient required dialysis with all 5 making a normal recovery with supportive care. The authors of this series pointed out that a relatively asymptomatic period may occur for several days before signs of acute renal failure become apparent.

The potential for delayed toxicity has been emphasized by another report of rhabdomyolysis in an adolescent with massive honey bee envenomation [12]. A 13-year old with several hundred stings was discharged after a period of observation in an ED, only to return several hours later with progressive edema and evidence of progressive rhabdomyolysis and renal dysfunction. Like our patient, his CK reached a peak at 48 hours (106,720 ng/mL), and labs were also notable for transient elevation of hepatic transaminases, anemia, and hypoalbuminemia. Betten et al warn that rhabdomyolysis, hemolysis, and hepatic transaminase elevation may occur within 24 hours, after a period of earlier and milder symptoms attributable to envenomation such as fatigue, dizziness, and gastrointestinal signs. The authors recommended that a child with greater than 1 honey bee sting per kilogram or an adult with >50 stings be monitored with observation and serial labs including creatinine phosphokinase levels.

Our patient demonstrates the potential for fire ant envenomation to lead to a well-described pattern of end-organ injury due to hymenoptera species. With the lack of evidence based predictive clinical characteristics for the development of a delayed hymenoptera toxidrome, a cautious approach to follow-up of patients with multiple stings, including fire ants, is warranted.

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