

An Anaphylactoid Reaction to Rattlesnake Envenomation in a Pediatric Patient

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Abstract: Rattlesnake envenomation causes a spectrum of symptoms and signs, many of which closely resemble an anaphylactic reaction. Development of airway compromise after a snake bite to an extremity is unusual, but has been previously reported. The majority of such reports detail a history of probable sensitization from previous contact with snakes or snake venom. Few reports exist without such previous contact; no reports are of pediatric cases. Here we present a 14-year-old boy with no history of prior snake exposure who presents with an anaphylactoid reaction after a rattlesnake bite.

Key Words: anaphylactoid, anaphylaxis, rattlesnake envenomation, crotalidae

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Rattlesnake bites are a common occurrence in the United States with a reported incidence of 5988 rattlesnake exposures over a 5-year period.¹ Envenomation typically causes a local reaction of ecchymosis, edema, and significant pain. Not uncommonly, systemic effects of hypotension and gastrointestinal symptoms are also seen. In severe envenomation, respiratory distress due to pulmonary edema may be seen. Airway compromise, however, is rare, occurring in only 1.7% of cases.² Most cases of airway compromise occur after repeated contact with snakes or their venom,^{3–9} likely due to anaphylaxis. Very few occur without such history,^{10–12} suggesting the possibility of an anaphylactoid reaction.¹³ We present the first pediatric case of an anaphylactoid reaction to rattlesnake envenomation.

CASE

A 14-year-old boy presented to the emergency department via emergency medical services with respiratory distress due to upper airway obstruction and gastrointestinal symptoms after a rattlesnake snake bite to his left lower leg. Before arrival to our facility, the patient experienced emesis, oropharyngeal swelling, labored respirations, and a hoarse voice. He was given intramuscular epinephrine 0.3 mg, intravenous ondansetron 4 mg, and intravenous diphenhydramine 50 mg. En route to the hospital, a second dose of intramuscular epinephrine was given due to persistent hoarseness and labored respirations.

On arrival to the emergency department, his initial vital signs included a temperature of 98.1°F, heart rate of 130 beats/min, respiratory rate of 23 breaths/min, blood pressure of 105/46 mm Hg, and oxygen saturation of 100% on a nonrebreather mask. On examination, he was pale and somnolent, but responsive. He

had mild tongue and facial swelling. His lungs were clear bilaterally without stridor or rales. His heart examination revealed a hyperdynamic precordium but no murmur or gallop. His abdominal examination was unremarkable. His extremity examination revealed 2 bleeding puncture wounds with surrounding ecchymosis on his left lower leg that was tender to palpation. His medical history included intermittent asthma as a younger child. He had no prior surgeries, allergies, nor took medication. He had no previous contact with rattlesnakes, including bites. He did report localized swelling after a bee sting 2 years prior. There was no family history of anaphylaxis, hives, or angioedema. Initial laboratory results were notable for a normal platelet count of $236 \times 10^3/\text{mm}^3$, international normalized ratio 1.2, PT 12.9 seconds, PTT 28.1 seconds, and mildly decreased fibrinogen of 170 mg/dL.

He was initially treated with an intravenous saline bolus (1 L), dexamethasone 10 mg, ondansetron 4 mg, and famotidine 20 mg. His oropharyngeal swelling resolved, but he began having episodes of emesis and diarrhea. He became hypotensive to 83/45 mm Hg with a heart rate of 146 beats/min. His vital signs improved while receiving 2 L of saline via push-pull method. He was loaded with 8 vials of Crotalidae Polyvalent Immune FAB (CroFab; Protherics Inc., Brentwood, TN) and admitted to the pediatric intensive care unit. On arrival to the pediatric intensive care unit his heart rate was 107 beats/min. He had a normal blood pressure of 125/61 mm Hg and oxygen saturation of 99% on room air. His emesis and diarrhea subsided and his mental status normalized. He received 4 more loading doses of CroFab (6 vials each) for progression of symptoms including local bruising, swelling, erythema, and mild coagulopathy (PT 16.3 seconds, fibrinogen 95 mg/dL). Three routine maintenance doses (2 vials) were then provided every 6 hours. He concurrently received solumedrol, famotidine, and diphenhydramine for 48 hours. These were discontinued without any recurrence of symptoms. The allergy/immunology service could not distinguish between anaphylaxis and an anaphylactoid reaction due to lack of a commercially available laboratory or skin test for detection of specific IgE to rattlesnake venom. On day 6 of hospitalization, he was discharged home with an epinephrine autoinjector.

DISCUSSION

Rattlesnake venom contains various proteins including proteolytic enzymes, metalloproteinases, phospholipase A2, toxic glycoproteins, histamine, and kinins that cause local and systemic effects.¹⁴ Reported local reactions include edema,¹⁵ ecchymosis, bleeding, pain, and bullae formation.¹⁴ Common systemic effects include gastrointestinal reactions such as nausea, vomiting, and diarrhea as well as nervous system toxicity including lethargy, weakness, and paresthesias. Severe envenomation causes consumptive coagulopathy and increased capillary permeability leading to cardiovascular instability and organ dysfunction or failure, including respiratory failure.^{12,14}

There have been reports of envenomation causing anaphylaxis.^{3–9} Anaphylaxis develops after an individual is sensitized to an allergen by a previous exposure resulting in production of IgE antibodies.

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Subsequent exposures may precipitate anaphylaxis as preformed IgE stimulates extensive mast cell degranulation and histamine release. In these cases, patients developed respiratory system dysfunction including dyspnea,^{3,4,7,9} wheezing,^{5,7,8} and oropharyngeal edema.⁶ Concurrent urticaria^{4,5,7,9} or angioedema^{3,4} was also observed in most cases. These reactions satisfy the diagnostic criteria for anaphylaxis.¹⁶ All of these cases involved a sensitizing history of either prior snake bites,^{4,5,7,8} extensive snake handling,^{3,9} or ingestion of rattlesnake meat.⁶ Furthermore, elevated venom-specific IgE levels have been demonstrated in patients with allergic manifestations to snake bites after previous exposure to snake venom.^{9,17,18}

Rarely, life-threatening respiratory distress has occurred without any history of sensitization. This anaphylaxis-like reaction, referred to as an anaphylactoid reaction, occurs without preformed IgE via an unclear mechanism.¹⁶ Two reports suggest such an occurrence from rattlesnake envenomation without previous exposure to rattlesnakes.^{10,11} Following a bite to a distal extremity, both patients developed oropharyngeal edema and respiratory distress. One patient also experienced urticaria.¹⁰ Resolution with subcutaneous epinephrine was observed in 1 case.¹¹ Epinephrine was ordered for the second case but was not administered due to delays in obtaining the medication. The anaphylactoid signs resolved after the patient received intravenous diphenhydramine, methylprednisolone, and antivenom.¹⁰

We present a case of a pediatric patient without any previous snake exposure who presented with edema to the face and oropharynx, a hoarse voice, and respiratory distress that resolved with epinephrine before the administration of antivenom. The quick response to epinephrine and the fact that the patient did not have other signs of severe systemic envenomation (eg, marked coagulopathy or protracted hypotension) suggest that this reaction was due to anaphylactoid mast cell degranulation. Although unlikely, we cannot definitively rule out true anaphylaxis due to antigen cross-reactivity to bee venom from a previous sting. This has been described in a patient following a bite by *Vipera berus*.¹⁸ To our knowledge, however, such cross-reactivity has not been demonstrated with Crotalidae envenomation.

We conclude that evidence continues to support rare cases of obstructive airway compromise after rattlesnake envenomation that satisfy the diagnostic criteria for anaphylaxis and anaphylactoid reactions. It is also important to emphasize that while the underlying pathophysiology of anaphylaxis and anaphylactoid reactions are different, the initial treatment should be the same. Thus, it is our opinion that prompt administration of epinephrine should be considered in the therapeutic regimen for snakebites when patients demonstrate any evidence of airway compromise.

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