Acute respiratory failure following scorpion stings: Anaphylaxis or severe systemic envenomation?

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ABSTRACT
Scorpion stings can cause a range of reactions which includes severe systemic envenomation resulting in respiratory failure, cardiovascular collapse, and severe neurologic complications. Patients with allergies to scorpion venom or allergies to bee and ant venom can have anaphylactic reactions following scorpion stings. We report a patient who developed severe respiratory distress following 2-3 scorpion stings on her face. She required an emergency cricothyroidotomy and prolonged hospitalization, related in part to underlying comorbidity. Physicians caring for patients following scorpion stings need to remember that these patients can have severe reactions to the venom, including anaphylactic reactions. The initial management likely involves respiratory and cardiac resuscitation. These patients may have a very difficult intubation and require an emergency surgical airway.

Keywords: scorpion, envenomation, acute respiratory failure, anaphylaxis

INTRODUCTION
Scorpions (e.g., Centruroides vittatus, the striped bark scorpion) are found throughout the United States, especially in the Southwest where the climate is dry and warm (Figure). Scorpion stings are generally considered non-life threatening. The National Poison Data System documented 15,604 reported stings in 2015; 1,416 required treatment at a healthcare facility. Outcomes were classified as none: 76, minor: 10,040, moderate: 698, major: 25, and death: 0.1

CASE
A 58-year-old woman presented to her local emergency department complaining of difficulty breathing; her husband told the physician that she was stung 2-3 times by a scorpion when she put on her BiPAP mask. She took diphenhydramine at home, but this did not relieve her symptoms. She had labored breathing with retractions and was making grunting noises. She also had a swollen tongue and throat, stridor, and diminished breath sounds; she had no skin rash. Vital signs included blood pressure 160/93 mmHg, heart rate 95 beats per minute, and respiratory rate 22 breaths per minute. Initial laboratory testing showed WBC 10.2 k/µL with 2.1% eosinophils, hemoglobin 13.4 gm/dL, and platelet count 284 k/µL. A complete chemistry panel results included sodium 140 mEq/L, potassium 3.6 mEq/L, chloride 104 mEq/L, BUN 15 mg/dL, and creatinine 1.0 mg/dl. Arterial blood gases included a pH 7.24, PaCO₂ 62 mmHg, and a PaO₂ 79 mmHg on a FiO₂ 100%. Oral intubation failed, and an emergency cricothyrotomy was done. She did not receive corticosteroids or scorpion antivenom.

The patient was transferred to University Medical Center in Lubbock, TX, using mechanical ventilation during transport. Her husband reported that she had allergies to aspirin, penicillins, doxycycline, nabumetone, and bee stings. Vital signs included blood pressure 89/63 mmHg, heart rate 90 beats per minute, and respiratory rate 16 breaths per minute. Her oxygen saturation was 96% on a FiO₂ of 45%. Initial
laboratory testing showed WBC 15.3 k/µL with 0% eosinophils, hemoglobin 12.4 gm/dL, and platelet count 225 k/µL. A complete chemistry panel included sodium 138 mEq/L, potassium 5.7 mEq/L, chloride 100 mEq/L, BUN 15 mg/dL, and creatinine 0.9 mg/dl. The patient received one dose of intramuscular epinephrine (0.3 mg), three days of norepinephrine by continuous infusion, and methylprednisolone followed by prednisone throughout the hospitalization. She also received famotidine for four days, diphenhydramine for two days, and albuterol-ipratropium for nine days. She required mechanical ventilation for eight days. ECG revealed episodic sinus bradycardia. Her echocardiogram was normal except for mild tricuspid regurgitation and an estimated right ventricular systolic pressure 43 mmHg (normal: <30 mmHg). She did not develop pulmonary edema, acute kidney injury, or any neurologic complications. The ENT service was consulted, and the patient underwent surgery to place a tracheostomy tube. The patient was eventually placed on a tracheostomy collar and discharged. She did not receive scorpion antivenom.

**Discussion**

Scorpion stings occur worldwide with the greatest incidences in subtropical and tropical regions. An epidemiologic study published in Wilderness and Environmental Medicine found that the clinical presentations depended on the species of scorpion and that severe complications included pulmonary edema, acute respiratory failure, cardiac arrhythmias, myocarditis, hypertension, hypotension, coma, seizures, and multiorgan failure. The study concluded that treatment generally includes three components: symptomatic measures, vital function support, and the administration of antivenom. The study also found that the patient prognoses were heavily dependent on the amount of time elapsed from the sting to the beginning of treatment.²

Scorpion venom contains numerous chemicals, including peptides, enzymes, mucoproteins, free amino acids, nucleotides, amines, lipids, heterocyclic components, inorganic salts, and other compounds.³ The toxic components of scorpion venom are small peptides that target ion channels found in both mammals and insects. The toxins that are the most clinically significant to mammals are the alpha-toxins which block voltage-gated sodium channels, leading to a prolonged depolarization and neuronal excitation. This stimulates both sympathetic and parasympathetic autonomic centers and releases epinephrine, norepinephrine, neuropeptide Y and endothelin-1.⁴ The parasympathetic effects of the venom are generally less severe than the sympathetic responses. Signs of parasympathetic involvement appear soon after the sting happens, and the patient may have bronchospasm, bronchorrhea, salivation, miosis, diarrhea, bradycardia, and diaphoresis.⁴ The sympathetic effects are often much more severe because of the additional effects of circulating catecholamines. Patients may develop myocardial injury, pulmonary edema, and cardiogenic shock. The blood pressure initially rises with an increase in cardiac output and then falls if there is a decrease in left ventricular function. Unlike the parasympathetic effects which appear quickly and subside, the sympathetic activity can persist for over 18 hours because of the release of catecholamines.⁴,⁵ Central nervous system effects are uncommon because the toxins cross the blood-brain barrier poorly. However, the venom in scorpions found in North America can cause severe neurologic complications, especially in children.⁶ These include severe agitation with uncoordinated arm flailing, ocular motor and visual abnormalities, and respiratory abnormalities, including increased secretions, airway obstruction, abnormal ventilatory control, and occasionally noncardiogenic pulmonary edema. The neurological complications may be due to hypertensive encephalopathy and catecholine release. Only about 10% of stings result in severe systemic envenomation; most of the time the sting causes erythema, edema, and paresthesias around the site of the sting.⁴

In healthy adults, scorpion stings rarely cause a medical emergency. Anaphylaxis from a sting is possible if the patient has been stung before or if there is a cross reaction to components in the venom related to prior insect stings. Nugent et al studied the cross reactivity of scorpion venom with imported fire ant venom and found significant cross-reactivity.
between these two venoms. Consequently, people with systemic reaction to imported fire ants are at a 20 fold higher risk for allergic reactions to scorpion venom.7 In addition, scorpion venoms have strong cross-reactivity with bee venom.8 The World Allergy Organization estimates that 1% to 7% of the general population have allergic reactions to insect stings.9 The CDC reports as many as 100 people in the United States die every year as a result of allergic reaction to insect stings.10 This number could be underreported because these deaths may be attributed to heart attacks, sunstrokes, or other causes. We think that our patient had an acute anaphylactic reaction to scorpion venom resulting in mucosal edema and upper airway obstruction. This reaction was most likely secondary to cross reactivity between scorpion venom and bee venom to which she had an allergy. The patient’s prolonged requirement for mechanical ventilation following tracheostomy was probably explained, in part, by her underlying sleep apnea syndrome complicated by pulmonary hypertension. The patient did not appear to have an associated toxic reaction due to the lack of rapid swelling at the sting site, nausea, diarrhea, lightheadedness, and muscle spasms.

Antivenom can be used in patients with scorpion stings; it binds to toxins so that they are unable to reach target sites. Its use has been controversial, and its low cost effectiveness typically limits its use to cases with severe systemic envenomation.11 Two studies showed that scorpion sting victims who received antivenom in addition to prazosin recovered much faster than those who received only prazosin.12,13 Unfortunately, by the time the patients have developed a severe envenomation reaction, the antivenom may not be very effective because it cannot reverse the injury already induced by the toxins.3 The antivenom needs to bind toxins before they are able to exert their effect and release catecholamines. Antivenom is a protein, so the risk of anaphylaxis is always present. Anaphylactic reactions to antivenom are due to either complement activation by IgG/residual Fc fragments or direct stimulation of mast cells.14 Within two hours the patient will develop itching, urticaria, dry cough, fever, nausea, vomiting, diarrhea, tachycardia, and abdominal colic.14 A minority of these patients may experience more severe symptoms, such as hypotension, bronchospasm, and angioedema. Some patients develop a delayed reaction following antivenom administration.15 There are no absolute contraindications to antivenom, but patients who have had reactions to horse or sheep serum in the past or have a history of atopic diseases are at a higher risk for severe reactions.14 Epinephrine is the treatment of choice in the event of an anaphylactic reaction, and promethazine has shown the most efficacy for prophylaxis.14 Serum sickness developed in 6% of patients receiving scorpion antivenom but they responded quickly to oral corticosteroids and/or antihistamines.15

In summary, scorpion stings can cause a range of reactions which includes severe systemic envenomation, resulting in respiratory failure, hemodynamic instability, and severe neurologic complications. These occur more frequently in children and depend on the scorpion species. In addition, some patients can have acute anaphylactic reactions to scorpion venom secondary to cross-reactivity from venoms from bees and ants. The initial management may require cardiopulmonary resuscitation and antivenom, if available. In adults, the clinical course is also influenced by underlying comorbidity.

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