Fire ants

Fire Ant, Brown Recluse Spider, Black Widow Spider and Scorpion Envenomations

By

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Introduction

This article will review the diagnosis and treatment of envenomations of four venomous creatures; fire ants, brown recluse spiders, black widow spiders and scorpions. Whether an individual clinician will commonly treat these envenomations depends on where in the country they are practicing. In the United States, antivenom for black widow spider and scorpion envenomations has helped reduce morbidity and mortality.

Fire Ants

Fire ants first were found in the United States in the 1930s. Now there are five times more fire ants per acre in the U.S. than in South America, as they escaped their natural enemies and thrived in the southern U.S.[1] There are two types of fire ants; the red fire ant named *Solenopsis invicta* and the black named *Solenopsis richteri*.[2] Red fire ants are typically found in the southeast

from Texas to North Carolina. There are areas of New Mexico, Arizona and California that are also infested.[1] The black fire ant is found in northern Alabama, northern Mississippi, and southern Tennessee.[2] Fire ants are remarkably hardy and can even form floating life rafts made of thousands of ants in times of flooding.[3]

Fire ants floating in flood water

Fire ant bites usually occur when their nest is disturbed, and occur mostly in the summer months. They can swarm with multiple fire ants stinging the victim, and if a fire ant mound is disturbed hundreds to thousands of fire ants may respond.[4] In addition, each ant can sting repeatedly within a very short time. When a fire ant stings its mandible locks onto its prey and venom is injected through a stinger located on the abdomen. It typically stings an average of seven to eight times while rotating its body in a circular pattern repeatedly stinging. Since fire ants hold on to the skin with their mandibles, they are not easily brushed off and often have to be pulled off individually.[4]

Fire Ant Venom

Fire ant venom is normally used to immobilize or kill prey the ants want to eat. The venom is a 95% water-insoluble alkaloid, with the rest being an aqueous protein solution. The alkaloid part of the venom has cytotoxic and hemolytic properties, while the protein portion may contain allergens.[2]

Fire Ant Envenomation[2,4]

In humans the initial response to the venom is a severe burning sensation. In a few minutes, after that subsides, a dermal flare and wheal occur and then within two hours papules form. Vesicles develop within four hours and by 24 hours these become sterile pustules. One way of identifying a fire ant envenomation is by these pustules that form after the sting. There is also a local reaction, which is characterized by erythema and edema which can be larger than ten centimeters in diameter, and can be very painful and pruritic, lasting from 24 to 72 hours. The skin reactions are IgE-mediated, and contain a dense fibrin gel that contains eosinophils, neutrophils, and lymphocytes. Anaphylaxis, may occur due to the allergens in the aqueous protein solution, more frequently in persons sensitized by a previous sting.

Fire ant stings

Treatment

Most patients stung by fire ants just require supportive care. Hydrocortisone cream, antihistamines and over the counter analgesics are typically all that is required initially. Ice packs may be helpful to relieve pain and swelling. The sterile pustules should not be opened. However, if they do open up they should be cleaned with soap and water and an antibiotic ointment may be used to prevent secondary infection. If a secondary infection does occur oral antibiotics may be needed. Occasionally, if there is a large local reaction a one-time dose of prednisone may be helpful. Anaphylactic reactions are treated in standard fashion.[2,4]

People who are severely allergic to fire ant stings can receive whole body extract immunotherapy, which contains the entire body of the ant, not just the venom as is typical treatment for other venomous insects. In whole body extract immunotherapy gradually increasing doses are administered which can reduce the risk of a future allergic reaction to fire ant venom.[4]

Brown Recluse Spiders

Brown recluse spider with violin marking on dorsum

The brown recluse spider or *Loxosceles reclusa*, is found mainly in the Midwest and Southcentral regions of the U.S.[5] It is also called the violin or fiddleback spider because of a violin-shaped marking on its back. An adult brown recluse spider with its legs extended is about 1 to 1.5 inches long.[6] They prefer dark areas such as under tree bark and rocks. Indoors they may be found in attics, closets, drawers or under bed sheets. These spiders generally only bite as a defense mechanism when they are crushed or pressed on.[5]

Brown Recluse Venom

The spider venom is cytotoxic and hemolytic and can cause a syndrome called dermonecrotic arachnidism.[5] Sphingomyelinase D is a major component of the venom that can cause hemolysis and activate the complement system. There are other proteases in the venom that

degrade collagen, fibronectin, fibrinogen, gelatin, and elastin basement membranes that have a synergistic effect with sphingomyelinase D leading to many of the skin findings detailed below. Hyaluronidase, alkaline phosphatase, esterase, and ATPase are also involved with the skin manifestations.[5]

Brown Recluse Spider Envenomation[5,6]

The initial bite is usually painless until two to eight hours later when the bite may become red, swollen and tender. The majority of brown recluse spider bites remain localized, healing within three weeks without serious complication or need of medical intervention. In more severe envenomations, the victim may develop a necrotic lesion appearing as a dry sinking bluish patch with irregular edges, peripheral erythema and frequently central pallor or a blister. An elevated lesion is not typical of a brown recluse bite. As the venom continues to destroy tissue, the wound may expand up to several inches over a period of days or weeks. The necrotic ulcer can persist for several months leaving a deep scar. Systemic symptoms such as chills, malaise, nausea, headache, dizziness and myalgias may also occur. In children, the elderly, or people with existing medical problems, the systemic reaction may be more severe and may include weakness, fever, joint pain, hemolytic anemia, thrombocytopenia, organ failure, disseminated intravascular coagulation, seizures, and death. In children, systemic symptoms may occasionally occur without skin findings and should be considered in the differential of acute hemolytic anemia in regions known to have the brown recluse spiders. Hemolysis has been reported up to seven days after a bite so follow up instructions should be given to parents of children even if there are no systemic findings during the initial visit.

Presumptive Brown Recluse Spider Bite

Diagnosis of Brown Recluse Spider Bites

Misdiagnosis of brown recluse spider bites is common. Frequently methicillin resistant staphylococcus aureus(MRSA) abscesses are misidentified as a brown recluse spider bite.[6,7] Unlike a brown recluse bite, MRSA abscesses may be crusted, purulent, and elevated.[7] A mnemonic, **NOT RECLUSE,** has been created to help physicians determine if a skin lesion is or is not from a brown recluse spider. The authors suggest that if two or more **NOT RECLUSE** signs are present, a brown recluse spider bite is a less likely cause of the lesion(s).[7]

N – Numerous - A typical recluse bite is a single lesion, but occasionally can be two bites. Multiple lesions indicate some other rash or insect bite.

O – Occurrence - Most commonly a recuse spider bite involves disturbance of the spider, in bed or hiding in a closet, attic or garage. If no such disturbance is noted, another diagnosis should be considered.

T – Timing - Recluse bites are most commonly seen from April to October, although occasionally they can be seen in the winter if the spider is disturbed. If the skin lesion occurs outside of this time frame, another diagnosis should be considered.

R – Red Center - A lesion with a red center is generally not a recluse spider bite. Due to tissue ischemia near the bite, the central part of the lesion will be pale, blue-white, or purple. There may be erythema around the lesion due to cytokine release.

E – Elevated - Recluse bites are generally flat or sunken. If the lesion is elevated another diagnosis should be considered.

C – Chronic - Most recluse bites, except those with a large amount of tissue destruction, heal within three months and it may be as little as three weeks for smaller lesions. Incomplete healing of the lesion suggests another diagnosis.

L – Large - The largest brown recluse bite injury generally does not exceed ten centimeters, although there may be a larger area of erythema around the wound. Very large lesions suggest another diagnosis, possible pyoderma gangrenosum.

U – Ulcerates Too Early - Recluse bites do not typically ulcerate until seven to 14 days after envenomation.

S – Swollen - Recluse bites typically do not cause massive swelling below the neck or above the feet. There may be significant swelling in recluse bites to the feet or eyelids. Swelling of lesions on the body suggests another diagnosis.

E – Exudative - With the exceptions of eyes and toes, recluse bites are not initially exudative, moist, or purulent. If pus is seen, another diagnosis hold be considered.

Treatment

Ice packs and arm elevation are initial first aid for brown recluse bites. Sphingomyelinase D has been shown to have less activity in colder temperatures.[8] Tetanus immunization should be updated if necessary.[5] Prophylactic antibiotics are not recommended.[9] Antihistamines may be used for itching.[5] There is one article in the literature by a physician who initially in his career did many surgical excisions for brown recluse bites and then he started prescribing antihistamines for seven to ten days. He reported that by using antihistamines in a series of 100 brown recluse bites, he did not need to perform any more surgical excisions. However, there does not appear to be any other clinical studies in the medical literature supporting this claim.[10]

While most brown recluse spider bites do not require any specific therapy, suggested therapies in the literature for more severe envenomations include dapsone, corticosteroids, antivenom, surgical excision and hyperbaric therapy. Unfortunately, there is a dearth of randomized studies of treatment modalities and some conflicting results. Antivenom is not currently available in the U. S., although there is one available in South America.[11]

Use of dapsone for brown recluse spider bites is controversial with conflicting animal studies, but is considered a therapeutic option. Its use is based on its ability to inhibit polymorphic leukocytes which ameliorates some of the venom's effects.[12,13,14] There may be serious side effects associated with the use of dapsone such as dose-related hemolysis, agranulocytosis, aplastic anemias, and methemoglobinemia.[15] Because of these potential serious side effects, dapsone should be reserved for adult patients who have rapidly progressing necrotic lesions. It is not recommended for use in children. Adults who are selected to receive dapsone should first be screened for glucose-6-phosphate dehydrogenase deficiency to prevent hemolysis.[15]

One study found no difference in wound healing between dapsone and brown recluse antivenom each alone or combined, although it was felt that dapsone had eliminated the need for surgical excision in some patients.[13]

Another animal study compared early surgical excision to delayed surgical excision after dapsone and found use of dapsone prior to surgery decreased scarring, complications and in one case the need for surgical excision.[14] They also found the use of corticosteroids or early surgical excision in an animal model were not effective therapies. If needed, surgical excision of a brown recluse lesion should be delayed until the wound edges are clearly demarcated. Skin grafting may be required for large lesions.[15]

Hyperbaric oxygen has been found in one animal study to reduce necrosis from brown recluse envenomation when administered within 48 hours, although other animal studies found no beneficial effect or just histologic improvement without obvious clinical benefit from hyperbaric therapy.[16,17,18] Hyperbaric oxygen has been postulated to decrease wound damage secondary to brown recluse envenomation in at least two ways. It is thought that wound damage is decreased in part because hyperbaric oxygen inactivates sphingomyelinase D by the disruption of

sulfhydryl groups. Hyperbaric oxygen therapy also increases the production of collagen by fibroblasts, thereby facilitating wound healing.[15] There are some animal studies and case reports that have demonstrated some improvement of brown recluse skin lesions with hyperbaric therapy both acutely, as well as in patients with non-healing wounds.[16,17,18,19]

Black Widow Spiders

Black widow spider with typical hourglass marking

In North America the Latrodectus species or black widow spider is a cause of significant envenomation. The spider can be identified by its black body and red hourglass-shaped marking on the abdomen. The black widow moniker results from observation of the female frequently devouring the male after a mating session. Black widow spiders typically range from 0.5 to 1.5 inches in length[20] and have fangs and venom. The female has larger venom glands, longer fangs, and can be many times larger in size than the male and as such is more of a threat to humans. Males may have red or yellow spots or bands on the back rather than an hourglass-shaped marking.[20]

The two species that most commonly cause envenomation within the United States are the *Latrodectus mactans*, or the southern black widow spider, found in the Southeast US and the *Latrodectus hesperus* or the western black widow spider, found in most of the Western U.S.[21] A third species *Lactrodectus variolus* or northern black widow spider is found in northern Florida up to the Middle Atlantic states and occasionally in southern Canada. In *variolus* species the red hourglass pattern on the female is typically separated into two distinct triangles.[20]

Black Widow Spider Venom

The venom of the black widow spider consists of a number of biologically active substances. Alpha-latrotoxin is the major component which binds irreversibly to receptors on presynaptic neurons. It causes an influx of calcium ions releasing massive amounts of neurotransmitters, which cause most of the symptoms in an envenomation.[21]

Black Widow Spider Envenomation

Black widow spider bites can occur while hiking, gardening, in garages, and frequently in outdoor bathrooms.[20] Fang marks may be seen and within minutes of being bitten there is pain, and the wound may become erythematous and edematous. There may be local diaphoresis around an area of central clearing. Severe muscle pain and cramping usually occur within an hour. Increased autonomic function leading to tachycardia, tachypnea and hypertension may occur.[21]

When patients develop systemic symptoms the term latrodectism is used. There may be diffuse muscle rigidity and cramping, tenderness, burning around the bite, truncal and abdominal tenderness, diaphoresis, headache, nausea, and vomiting.[21] Occasionally black widow bites have been misdiagnosed as an acute intra-abdominal emergency such as appendicitis due to the muscle pain and rigidity.[22] The pain associated with latrodectism spreads from the bite site, so if someone is bitten on the foot the pain will initially move proximally up the leg and then to the rest of the body. Lab values are generally non-specific but may show an elevated white blood cell count, hematuria, and elevated liver enzymes. Occasionally rhabdomyolysis or myocarditis may occur.[21]

In one case series of over 23,000 exposures to black widow venom, 65% of patients presented with minor clinical effects, 33.5% moderate effects, and 1.4% had major potentially life-threatening symptoms.[23]

Treatment

Initial management of black widow envenomation includes local wound management, ice packs, and tetanus prophylaxis. Calcium gluconate and methocarbamol, which were recommended in the past for the resulting muscle spasms have been shown to be ineffective and are no longer recommended. Pain management may be required with oral analgesics and occasionally opioids. Benzodiazepines may be required for muscle spasms.[21]

There is an antivenom that can be used for cases of latrodectism that is very effective but allergic reaction, serum sickness, and anaphylaxis may occur as it is made out of horse proteins.[24] The drug information sheet recommends a skin or conjunctival test be performed prior to administration to check for allergies. The dose is one vial intravenously which can be repeated if needed.[25] A more purified antivenom is currently in clinical testing to reduce the possibility of allergic reactions, but is not available commercially yet.[26,27]

The prognosis for black widow bites is good. Most pain and systemic symptoms are self-limited and recovery is typically within 24 to 48 hours.[21]

Scorpions

riped bark scorpion ready to sting

St

Female bark scorpion carrying newborn babies

Poison control centers in the United States receive close to 17,000 reports of scorpion envenomations per year.[28] There are over 1,700 scorpion species around the world but only 25 are lethal to humans. In the United States there are a number of different species but there are two that cause most significant envenomations. The most common is *Centruroides sculpturatus*, followed by *Centruroides vittatus*.[29] There has been some taxonomic confusion in the past with *Centruroides sculpturatus* and *Centruroides exilicauda* being considered the same species and the names used interchangeably in the literature. However, research has concluded they are two separate species.[30] The *Centruroides sculpturatus* is also known as a bark scorpion for its ability to climb and can be found in trees, rock walls or house walls as well as under rocks or in crevices. The *Centruroides vittatus* is also known as the striped bark scorpion due to the marking on its back. Both species are found in Arizona, New Mexico, Texas, California, Utah, Nevada, and in adjacent areas of Mexico.[31.32] The *Centruroides exilicauda* is found in Mexico and is also known as the Baja California scorpion. Its venom is much less toxic to humans than the other two species.[30]

Scorpion Venom[29,31]

An adult scorpion is typically two to three inches long,[31] with a stinger on its tail which it uses to paralyze prey to make it easier to eat. It also will sting predators(and humans) when threatened. Infants and children are more sensitive to the neurotoxin than adults. Adults are stung more often than children, however children more frequently suffer from severe illness. Scorpion's venom is composed of multiple neurotoxins, an ACE inhibitor, and a component that inhibits platelet aggregation. The neurotoxins inhibit sodium channels of the peripheral nervous system, causing a prolonged membrane action potential and allowing repetitive axonal firing.[32] Symptom onset is typically within a few minutes after the sting and progresses to its maximal effect within five hours. Patients with only localized symptoms can be safely discharged home if there is no progression of the disease after observation for those five hours. There have been no reported deaths from scorpion envenomation in Arizona since 2013.[28]

Scorpion Envenomation[29,32]

A grading system has been developed to categorize and assist in the treatment of scorpion stings.

Grade I envenomation causes local pain and paresthesias at the sting site. The puncture wound may not be visible. The sting does not usually produce a local inflammatory reaction, making diagnosis in young children and infants difficult. The "tap test" may confirm a provider's suspicion of a sting by *sculpturatus* by tapping on the area of the sting, causing increased pain. This may not occur with other scorpion species. Supportive care and analgesia are all that is typically required.

Grade II envenomation causes local pain and paresthesias at the site of the sting as well as proximal to the sting site. Occasionally there may be radiation to contralateral extremities. Care includes analgesia and possibly anxiolytics if needed.

Grade III includes Grade II symptoms with added cranial nerve and bulbar dysfunction (increased oral secretions, blurry vision, rapid tongue movement, nystagmus), or skeletal neuromuscular dysfunction with flailing of the extremities, opisthotonos (tetanus-like hyperextension of the head with arching of the back), or emprosthotonus (forward flexion of the head and feet toward each other) being possible. Autonomic dysfunction may also occur and most commonly symptoms include salivation, vomiting, bronchoconstriction, diaphoresis, and tachycardia. Grade III envenomations can sometimes adversely affect a patient’s airway. In pediatric patients common findings are restlessness, writhing, opsoclonus (uncontrolled chaotic rapid eye movements), tachycardia, and hypersalivation. Patients with Grade III stings generally require analgesia and anxiolytics as well as antivenom.

Grade IV envenomations includes both cranial nerve and skeletal muscle dysfunction, which can lead to hyperthermia, rhabdomyolysis, pulmonary edema, and multiple organ failure. Antivenom will be required.

Treatment

Grades I and II envenomations generally just require supportive care, ice packs, tetanus immunization if needed, analgesia and possibly anxiolytics.[29,32]

For Grades III or IV envenomation antivenom and hospital admission may be required. In 2011 Anascorp Centruroides (scorpion) immune $F(AB)_2$ was approved by the FDA, which contains purified fragments of immunoglobulin G that bind and neutralize venom. A typical dose is three to five vials. It is made from horse serum so serum sickness, allergic reactions, and anaphylaxis may occur.[33] Without antivenom, the average time to resolution of symptoms is approximately 30 hours. In one small study of 15 critically ill children, 100% of the antivenom treated patients had resolution of symptoms within four hours versus 14% in the placebo group.[34] Typically, about 2% of all scorpion envenomated patients will require antivenom.[28]

Conclusion

Fortunately, most of the envenomations from fire ants, scorpions, black widow and brown recluse spiders are not severe. However, severe systemic toxicity can occur with all of them. Deaths are rare, especially with the availability of antivenom for black widow spider and scorpion envenomations. Disfiguring scars with deep tissue penetration are possible with brown recluse spider bites. Treatment protocols for severe brown recluse spider bites are hampered by a lack of good scientific evidence, although ice packs, dapsone in adults, hyperbaric therapy and delayed surgical excision, if needed, are most frequently recommended. Antihistamines may help with itching and there is one anecdotal case series, not confirmed by other studies, where the author suggested that antihistamines may help with wound healing.

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