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SUSPECTED BROWN RECLUSE ENVENOMATION: A CASE REPORT AND REVIEW OF DIFFERENT TREATMENT MODALITIES

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□ **Abstract—Background: The *Loxosceles reclusa*, commonly known as the brown recluse spider, is responsible for virtually all cases of spider bites leading to a significant necrosis. Case Report: We report the case of a 72-year-old man who presented to the Emergency Department complaining of back pain, weakness, and diarrhea. The patient stated that he sustained a bug bite 1 week before presenting to the hospital. His wound was necrotizing in nature and after an exhaustive work-up, the most likely etiology was found to be envenomation by a brown recluse spider, *Loxosceles reclusa*. Conclusion: This is an endemic cause of a necrotizing wound bite in areas of the Midwestern and Southern United States, but it is rarely reported in the Northeast.** © 2011 Elsevier Inc.

□ **Keywords—recluse; envenomation; spider; wound; infection**

INTRODUCTION

There are several species of *Loxosceles* spiders in the United States; the most common and dangerous being *Loxosceles reclusa*, commonly known as the brown recluse spider (BRS). BRS bites are responsible for virtually all cases of spider bites leading to a significant necrosis, however, some authors suggest that the only way to definitively diagnosis a BRS bite is to identify the spider itself, which is often not available (1). BRS bites occur most often in the Midwest from Nebraska to Ohio, and the South from Georgia to Texas (2). Although all spiders are poisonous, most species do not have large enough fangs to penetrate human skin. Most bites tend to heal without medical treatment, whereas some lead to necrotic lesions and, rarely, bites may lead to a systematic illness known as Loxoscelism. Loxoscelism is not a reportable illness, making nationwide tracking difficult. In endemic areas where the BRS population is dense, envenomation is infrequent, leading many to believe that the occurrence of bites in non-endemic areas is even less likely (3,4). Many lesions attributed to the BRS actually result from other causes, making these bites appear more common than their actual incidence (3,5,6) (Table 1).

A typical bite exhibits a characteristic pattern that includes pruritis, pain, and erythema within 6 h, and an irregular, erythematous ring that demarcates the bite by 24 h. In more severe cases, necrosis can be seen within 48–72 h. Early signs of necrosis are hyperesthesia, bullae, and cyanosis, leading to an ulcer that is red-blue in color, painful, and covered by an eschar. The severity of the lesion does not correlate to developing systematic Loxoscelism (Table 2). Rare but dangerous complications of BRS bites include pyoderma gangrenosum, intravascular hemolysis, renal failure, pulmonary edema, and systemic toxicity. Wendell states that only 10–15% of bites lead to "major problems" that were

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Table 1. Differential Diagnosis for BRS Bites

Bacterial skin infections (*Staphylococcus* or *Streptococcus*), community-acquired MRSA
Fungal skin infections
Viral skin infections (Herpes simplex or zoster)
Pyoderma gangrenosum
Erythema multiforme
Diabetic ulcer
Lymphomatid papulosi
Poison ivy or oak
Squamous cell carcinoma
Localized vasculitis
Syphilitic chancre
Adverse drug events
Other bites
Thromboemboli
Lyme disease
Chemical burns
Necrotic fasciitis
Anthrax
Rhus dermatitis
Decubitus ulcers
Stevens-Johnson syndrome

BRS = brown recluse spider; MRSA = methicillin-resistant *Staphylococcus aureus*.

defined as unacceptable scarring, hospitalization, or chronic lesions (3).

Identifying the spider itself is considered to be the only conclusive way to diagnose a BRS bite. The BRS is commonly described as having a violin-shaped or fiddle-like brown marking on its dorsal surface (Figure 1) (7). This marking, however, is not unique to the BRS species. A more distinguishing feature is the number of eyes. Whereas most spiders have eight, *L. reclusa* has six eyes arranged in a distinctive pattern of three pairs, known as dyads, with one pair in the front and the other two pairs on the side of the cephalothorax (Figure 2) (8). They are nocturnal and are considered to be house spiders, as their habitat includes attics, basements, boxes, sheds, and woodpiles. The spiders are not known to migrate out of their native areas, but may be moved from place to place by humans, leading to reports of bites in non-endemic areas (3,5,9).

In this review, we performed a literature search for current trends in the treatment of BRS bites. We hope to provide clarification of possible treatment methods for the clinician who is presented with a suspected BRS bite.

Table 2. Signs and Symptoms of Systemic Loxoscelism

Fever up to 40.5°C (105°F)
Chills
Myalgias/arthralgias
Nausea/vomiting
Thrombocytopenia
Hemolysis
Disseminated intravascular coagulation
Death

Figure 1. Fiddle-shaped marking on dorsal surface of *L. recluse* (7).

CASE REPORT

A 72-year-old man was brought to the emergency department (ED) complaining of back pain, weakness, and diarrhea. The patient was noted to have a wound on the right side of his upper back, which he stated occurred from a "bug bite" 1 week before his hospital visit. The wound progressed during the week and was the size of an egg when he presented to the ED. The wound was extremely painful to touch, pruritic, and not relieved with

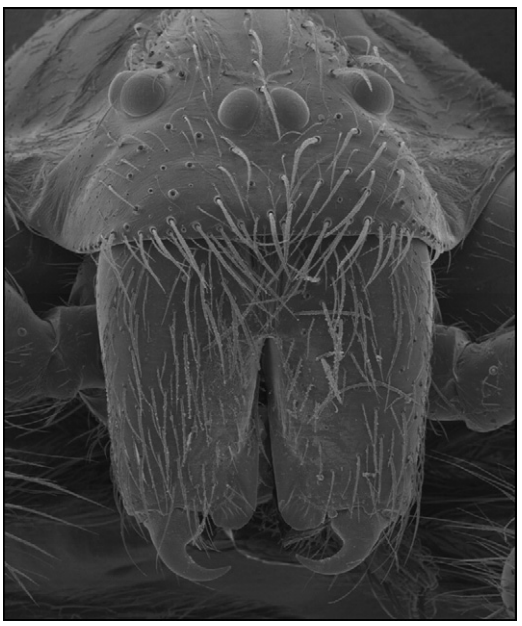

Figure 2. Dyads distinguishing *L. recluse* (8) (copyright Dennis Kunkel Microscopy, Inc.; reprinted with permission).

any medications. He denied any fever or chills, night sweats, nausea, or vomiting. The patient had a past medical history significant for coronary artery disease, benign prostatic hypertrophy, hyperlipidemia, and hypertension. His past surgical history was significant for a right carotid endarterectomy and pacemaker placement.

On examination, he looked to be in distress secondary to the pain he was experiencing. There was an ulcer on the right side of his upper back that was approximately 7×7 cm with erythema and induration, and containing a 3×3-cm necrotic area in the center. The ulcer was red-blue in color, painful to touch, and the necrotic center contained a dark eschar. Laboratory results showed a normal white blood cell count of 9.3×10^9/L. The patient had a normal hematocrit of 40.9% and an international normalized ratio (INR) of 1.14.

Due to the necrotizing nature of the wound, the patient was taken to the operating room for debridement. The wound was widely debrided to the fascial layer with removal of necrotic debris. During surgery, it was determined that there was no involvement of the fascia. The wound was then packed openly, placing loose stitches for primary closure.

The patient was then transferred to the floor for further care. Repeat laboratory results 3 h after the surgery demonstrated that the patient's hematocrit had decreased to 28.9% (from initial hematocrit of 40.9%). The patient's INR had also increased to 1.45 (initial INR was 1.14). He became hypotensive with a systolic blood pressure in the 80s. The patient was resuscitated with one unit of packed red blood cells, two units of fresh frozen plasma, and 2 L of 0.9% normal saline. The wound was also reopened, a large blood clot was removed, and the bleeding was controlled with cauterization. He was then transferred to the intensive care unit.

Repeat laboratory results showed that the patient's hematocrit decreased to 27.0%. The patient was given multiple units of blood until his hematocrit stabilized to 31.0%. The patient's systolic blood pressure also remained in the 120s throughout the rest of his hospital course. Dressing for the wound site was changed daily for the next few days. At this point it appeared that the wound was clean, and it was closed secondarily with sutures.

The typical BRS bite exhibits a characteristic pattern including pruritis, pain, and erythema, and an irregular, erythematous ring demarcating the bite. Within 24–72 h, a single clear or hemorrhagic vesicle develops at the site that later forms a dark necrotic eschar. Our patient presented with very similar signs and symptoms, however, no spider was actually seen. It is possible the wound may have occurred from another source, but a BRS bite would closely match this patient's clinical presentation. Systemic symptoms may include generalized weakness and diarrhea, which were also found in our patient.

DISCUSSION

Most BRS bites heal without aggressive medical treatment. Bites may be cleaned and treated with "RICE" (rest-ice-compression-elevation). Mild bites may be treated symptomatically with aspirin and antihistamines. Tetanus status should be updated as with any penetrating wound. It has been suggested that bites with tissue breakdown should be treated prophylactically with antibiotics such as a cephalosporin. Systemic Loxoscelism can be treated supportively with hydration, and monitored with serial blood counts and electrolytes. Steroids have been used to prevent kidney failure and hemolysis, but their efficacy is subject to debate (5). One must also consider the possibility of secondary infection to the bite site as the cause of presenting symptoms and not the bite itself when choosing a treatment regimen (6). Other treatments that are often associated with BRS bites include: dapsone, hyperbaric oxygen, nitroglycerin, electric shock therapy, and surgical excision.

Dapsone

Dapsone has long been suggested in the treatment of brown recluse spider bites resulting in necrotic lesions. It is thought that its polymorphonuclear leukocyte-inhibiting effects prevent chemotaxis and thus limit the inflammatory response at the wound site. Many adverse side effects have been attributed to dapsone, including: dose-related hemolysis, sore throat, pallor, agranulocytosis, aplastic anemia, cholestatic jaundice, methemoglobinemia, peripheral neuropathy, and hyperbilirubinemia. Many of these side effects overlap with Loxoscelism and may confuse the clinical picture. Dapsone cannot be used in patients with glucose-6-dehydrogenase deficiency, as these patients already have an increased risk of hemolysis. Researchers who support its use recommend that it be reserved for moderate to severe or rapidly progressing cases only, and never used in children (3,5,10). As few human studies have been conducted, the use of dapsone remains controversial due to its questionable efficacy and significant side effect profile.

Multiple studies in different animal models have been performed comparing dapsone use against controls and other treatment modalities. These studies have shown conflicting results. Rees et al. compared early surgical excision vs. dapsone and delayed surgical excision in a prospective study of 31 human patients who chose which treatment group to which they would be assigned (11).

There were no controls. The researchers reported that the dapsone and delayed excision group fared better than the early excision group with decreased scarring and wound complications. They postulated that pretreatment with dapsone not only decreased surgical complications, but improved outcome. This study has some inherent weaknesses. There was no blinding of the study on the part of the investigators or the human subjects, introducing a possible bias. There was also no control group, so it is not known whether the improved outcome of dapsone and delayed excision was due to the use of dapsone or to the delay of surgery until the wound fully evolved. To say that the improved outcome in this study was due to dapsone or to support its use in humans for the treatment of BRS bites is premature.

Barrett et al. tested dapsone against control and electrical shock in a prospective, placebo-controlled, experimental trial in the guinea pig model (12). Their results showed that the dapsone therapy group demonstrated significantly less induration and necrosis than the control group and other treatment groups, concluding that dapsone therapy is more effective than electrical shock or no treatment in the guinea pig model. The significance or validity of this study for humans is unclear, as it employed a guinea pig model. Most studies use the porcine model due to the pig's skin similarity to human skin, or the white rabbit due to its clinical course of BRS bites being similar to humans. Barrett's study also ended 3 days after envenomation, thus, the full evolution of the lesion cannot be truly evaluated. The "dapsone effect" reported here may wear off and show no change in clinical outcome.

Phillips et al. demonstrated in a randomized, blinded control study that dapsone had no significant effect on lesion or ulcer size, or histopathology in the white rabbit model compared to control and the other treatment modalities of hyperbaric oxygen and cyproheptadine (to be described later) (13).

Hobbs et al. compared dapsone to control and to hyperbaric oxygen in a randomized, controlled study using the swine model. They reported that no significant change was noted in necrosis or induration on days 1–7 of the experiment. Their results did show a decrease in induration, but only on days 7 and 14, between all treatment groups and the control, which has unknown clinical significance. They concluded that there was little clinical benefit to treatment with dapsone, hyperbaric oxygen, or a combination of both treatment modalities (14).

Hyperbaric Oxygen

The study of hyperbaric oxygen (HBO) in the treatment of BRS bites has produced even more conflicting results. HBO has been postulated to be beneficial in the treatment of necrotic lesions through multiple mechanisms. HBO may promote angiogenesis at the lesion site, leading to a decrease in the severity of the wound and an increase in the rate of healing. The extent of envenomation is decreased by directly inactivating the brown recluse venom due to its chemical structure. It is known that HBO inactivates sulfhydryl groups, and the necrotizing component of BRS venom is thought to contain this group (15). HBO may also cause pulmonary sequestration of polymorphonuclear lymphocytes, thus decreasing the inflammatory response.

The side effect profile of HBO includes barotrauma, particularly to the ears, sinuses, and lungs, with oxygen toxicity being another concern. Also a consideration is the cost of HBO treatment and the possible claustrophobia experienced while in the chamber (15). Svendsen presented a series of case reports demonstrating the positive effects of HBO on the necrotic bite of the BRS (16). HBO was used adjunctively to steroids, antibiotic, and antihistamines in this series. The bite was presumptively diagnosed because it was not indicated whether or not the spider was identified. Svendsen reported that the patients received symptomatic relief of pain, and wounds healed without any scarring or with minimal scarring. A possible selection bias exists, as HBO was started in those cases that looked to be problematic or heading to third-degree sloughing. Due to the nature of the study, no control was available for comparison.

Maynor et al. looked at 14 adult patients with presumed BRS bites (15). The patients were all treated with HBO for an average of seven treatments. The researchers reported that all patients healed without scarring or disability or the need for skin grafting. They concluded that this small series suggests a beneficial role for hyperbaric oxygen in dermonecrotic lesions of *L. recluse* (15). Although it is desirable to see the outcome of treatment in human models, this study had multiple weaknesses. The sample size was small and the clinical course may not adequately represent the typical course of a BRS bite. The study was not blinded, nor was there a control group. The study does not indicate the time course of healing and does not take into account that most likely the wounds would have healed on their own without treatment. Based on these questions that were not taken into account in this study, it is difficult to see the beneficial effect of HBO here.

In another study by Maynor, the investigators looked specifically at hyperbaric oxygen against control using different combinations of HBO treatment in a nonblinded, prospective, controlled white rabbit study (17). This study specifically looked at immediate and delayed HBO administration vs. control. The investigators reported that HBO had no effect on wound blood flow.

Both immediate and delayed HBO treatment significantly decreased wound diameter at 10 days, whereas normoxic gas under hyperbaric conditions had no effect, though all wounds had evidence of necrosis. They concluded that HBO within 48 h of a simulated bite resulted in a significantly smaller wound. This study was not blinded and may have introduced bias into the study. Also of note were two reported fatalities, which were then excluded from data collection.

In a study by Strain et al., the effects of hyperbaric oxygen on brown recluse spider envenomation were studied in three treatment groups in white rabbits (18). The groups consisted of a control, HBO once daily starting 72 h after envenomation, and HBO twice daily starting 72 h after envenomation. The investigators concluded that there were no significant effects of HBO treatment on lesion healing as measured by lesion area. However, when histologic evaluation was conducted at 24 days post envenomation, the twice-daily HBO treatment group showed enhanced recovery at the histologic level compared to once-daily treatment and control, but no superficial differences were seen among the groups. Although the histological results may suggest some benefit to hyperbaric oxygen treatment, it is questionable as to the clinical significance.

In the study by Hobbs et al., the effects of hyperbaric oxygen treatment were investigated against dapsone and control (14). Based on the results, they concluded that hyperbaric oxygen or a combination of hyperbaric oxygen and dapsone offers little clinical benefit in *Loxosceles* envenomation.

In a study by Phillips et al. that was mentioned above, dapsone, hyperbaric oxygen, and the antihistamine cyproheptadine treatments were investigated and compared to control in a randomized, blinded, controlled study of white rabbits (13). The total lesion size and ulcer size were followed for 10 days, and then studied for histopathology. The investigators reported that the groups did not differ significantly with respect to lesion size, ulcer size, or histopathological ranking. The researchers concluded that they could not recommend any of the treatments studied in the treatment of *Loxosceles* envenomation. Weaknesses in this study included the opportunity for bias, as the tracings of lesions were compared by the lead investigator without blinding. Pathology, however, was blinded to the treatment groups.

Nitroglycerin

The use of nitroglycerin as a treatment modality for brown recluse spider envenomation has been suggested and has anecdotal case reports as evidence for efficacy. Local vasoconstriction and platelet plugging contribute to tissue death and ischemic necrosis. The local vasodilatory effects of nitroglycerin may lessen these effects and decrease the extent of the lesion.

Burton claims that he has used nitroglycerin patches for 10 years and reports that the reverse vessel spasm can prevent ischemic damage and, when used within 48 h of a bite, can prevent ulceration (19).

Lowry et al. assessed the effects of nitroglycerin on BRS bites in a randomized, blinded, controlled study in the white rabbit model (20). Nitroglycerin paste was applied to the envenomation site every 6 h for 3 days. Gross examination and measurement of the lesions was conducted once daily for 10 days. Serum markers were also evaluated on days 0, 5, and 10 to monitor for systemic side effects. The investigators reported that lesion areas between control and intervention groups were not different over time. The mean areas of the control group were significantly higher at 24 and 48 h, but there was no difference on other days. The inflammation score was also higher in the treatment group, suggesting a possible increase in systemic occurrence of envenomation. They concluded that topical nitroglycerin did not prevent necrosis, and its use is not supported. In fact, its use may increase systemic side effects.

Electric Shock Therapy

The use of electric shock therapy in the treatment of BRS envenomation has been suggested due to its use in the early therapy of venomous snakebites. Osborn reports on 147 cases of confirmed and suspected BRS bites (21). In this series, Osborn reports that in the 127 cases in patients who completed follow-up, lesion excision or grafts were not necessary. In this series, pain and systemic symptoms were usually improved in 15 min, and the shock arrested the progression of venom damage. Although this case report offers anecdotal evidence for the use of electric shock therapy, there are too many weaknesses inherent in this type of study to recommend its use. Specific to this study is the high number of unconfirmed bites, leading to a selection bias in the study. None of the participants was blinded, and a placebo effect has to be considered when discussing symptomatic relief of pain. The lack of a control group, again inherent to this type of study, makes it impossible to evaluate whether or not these wounds would have healed without intervention.

Barrett et al. looked at dapsone and electric shock therapy in a study described above (12). Two different types of stun guns with different administration of electricity were used. Treatment began 16 h after inoculation and lasted for 3 days, with lesion area measurements made for those 3 days. The investigators reported that

dapsone resulted in less induration and necrosis compared to the control and stun gun groups. There were no advantages to the electric shock compared to control after 72 h following envenomation. Their conclusions on dapsone are mentioned above, but they could not find a benefit in the electric shock groups compared to control. The investigators did mention that all wounds healed regardless of therapy.

Surgery

Some researchers recommend surgical debridement for large wounds. Although surgical techniques vary, there seems to be consensus that surgery should not be performed for at least 6–8 weeks until the lesion has been stabilized. Earlier surgery can lead to an increase in inflammation and may increase the effects of the venom (5). This is supported by the report by Rees et al. previously discussed (11). According to this study, delayed excision with dapsone demonstrated a definite advantage over early excision, with increased rate of healing and decreased complications.

CONCLUSION

Most *Loxosceles* lesions will heal without treatment. Many conditions can mimic the symptoms of BRS bites, and most treatments are controversial and have side effects. The studies we have reviewed have not conclusively shown that the treatments used significantly alter the natural outcome of the bites (22). We cannot at this time recommend dapsone, hyperbaric oxygen, nitroglycerin, electric shock therapy, or surgical excision as treatment options. It is certainly possible that well-controlled human studies may prove efficacy for some of these treatments in the future.

Reports of unverified lesions may contribute to the assumption that BRS bites are more common than they truly are (4,23,24). This may lead to unnecessary and harmful treatments as well as increased side effects and complications (24). It is especially important for physicians in non-endemic areas to recognize these facts and to not over-diagnose or over-treat BRS bites.

When presented with a suspicious necrotic lesion, the physician must first consider the differential diagnosis; treatment decisions should then be based on the symptoms. Supportive care and careful observation should be the first-line therapy. We feel that it is safe to recommend cleaning wounds and treating symptoms with RICE, aspirin, and antihistamines, and updating tetanus status as needed. It is important to watch for tissue breakdown and symptoms of secondary infection and to consider treating with antibiotics. Be aware of the possibility of systemic Loxoscelism, consider treating supportively with hydration, and monitor with serial blood counts and urinalysis in severe cases. There has been success at identifying *Loxosceles* venom by enzyme-linked immunosorbent assay, but a sensitive and specific test needs to be developed to help aide physicians in making a diagnosis in unlikely patients in non-endemic areas (25).

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