Rattlesnake Envenomation and Compartment Syndrome: A Case Study
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Citation

Abstract
A 27–year-old male presented to the Emergency Department after suffering a rattlesnake bite with envenomation to his left lower leg. After admission to the medical-surgical floor, his pain and swelling increased and a surgical consult was obtained. The diagnosis of acute compartment syndrome was made based on the clinical presentation of the patient and he was taken to the operating room for an emergency fasciotomy. This article describes the evidence-based management of a patient with compartment syndrome as a result of rattlesnake envenomation.

INTRODUCTION
Venomous snake bites to humans remain a concern to all practitioners employed in the Emergency Department (ED). Deaths related to snake envenomations have been estimated to cause more than 10,000 fatalities annually worldwide. In the United States (US), where reporting of snake envenomations is not mandatory, it is difficult to concretely define both the number of envenomations annually and the mortality associated with these occurrences. However, the states with both the highest number of reported envenomations and highest rates of morbidity and mortality are Texas, Florida, and Georgia. According to the Texas Department of State Health Services, over 7,000 venomous snake bites occur in the US annually resulting in two deaths in Texas each year. For the period of 2000-2007, a 27% increase in envenomation of venomous snakes to Poison Control Centers occurred. Up to 99% bites are caused by snakes in the Crotalidae family, which includes the various rattlesnake species. In Texas alone, eight different types of rattlesnakes exist. While only a small number of deaths occur from poisonous snake bites, the number of complications that are a result of these bites can be debilitating and life altering.

Most venomous snake bites occur from April to October when the snakes are most active and are breeding. While this clinician has treated many snake envenomations over the past 13 years, the featured case was unique. The patient received early and appropriate care in the ED but progressed to the development of compartment syndrome and had to be taken to the operating room (OR) for emergency fasciotomy. The purpose of this case presentation is to identify the evidence-based treatment of compartment syndrome that develops from pit viper envenomation.

CASE PRESENTATION
HISTORY OF PRESENT ILLNESS
A 27-year-old male who was admitted to the surgical floor after suffering a rattlesnake bite approximately eight hours ago is now complaining of severe and persistent pain. The pain is increased and unrelieved by his pain medication regimen, and increased swelling has occurred to his left lower leg. He was initially treated in the ED after the snakebite, where the physician on duty felt that the envenomation warranted the use of antivenom. The patient was seen by general surgery at the time of admission, and the antivenom protocol was continued on the floor on admission. The orthopedic surgeon was consulted for a second opinion on the possibility of the development of compartment syndrome.

PAST MEDICAL AND SURGICAL HISTORY
No significant medical history
Tonsillectomy at age 8, appendectomy at age 16, arthroscopic surgery of the right knee at age 24

ALLERGIES
No known drug allergies
SOCIAL AND FAMILY HISTORY
Social history included a pack-per-day history for nine year and alcohol consumption of 12 to 24 beers per weekend. He denied any history of the use of illicit drugs. He is currently unmarried and has no children. His current employment is as a roughneck for a drilling company, which he has been employed at since the age.

Maternal history positive for hypertension and diabetes; paternal history is unknown

CURRENT MEDICATIONS
None

PHYSICAL EXAM
Vital Signs: Temperature of 99.6°F orally, pulse 121 beats per minute, respiratory rate 20 breaths per minute, blood pressure 100/52 mmHg, oxygen saturation 98% on room air.

Extremities: Obvious swelling and ecchymosed left lower leg with puncture wounds consistent with a rattlesnake bite.

Neurological: Grossly intact, two-point discrimination altered between the great and second toe of left foot.

General/Constitutional: Well nourished and appearance congruent with stated age. Appears anxious and in pain, but in no acute distress. Remainder of the physical exam grossly normal except as stated above.

LABORATORY DATA (SEE TABLE 1)

<table>
<thead>
<tr>
<th>Test</th>
<th>Abnormal Result</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Blood Count</td>
<td>15.9 x 10^6</td>
<td>4.5-11.0 x 10^6</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>118 g/dL</td>
<td>135-175 g/dL</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>34.3%</td>
<td>29-49%</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>84.2%</td>
<td>5% – 70%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>2.6%</td>
<td>1% – 5%</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>31 mL/dL</td>
<td>22.5-40 mL/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>118 x 10^12</td>
<td>150-450 x 10^12</td>
</tr>
<tr>
<td>Total Creatinine</td>
<td>7.48 mg/dL</td>
<td>0.6-2.4 mg/dL</td>
</tr>
<tr>
<td>Protein</td>
<td>5.8 g/dL</td>
<td>6.0-8.0 g/dL</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.4 g/dL</td>
<td>3.5-5.5 g/dL</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>180 mg/dL</td>
<td>150-400 mg/dL</td>
</tr>
<tr>
<td>PT</td>
<td>15.9 seconds</td>
<td>11-15 seconds</td>
</tr>
<tr>
<td>PTT</td>
<td>16.7 seconds</td>
<td>20-35 seconds</td>
</tr>
<tr>
<td>INR</td>
<td>1.3</td>
<td>0.9-1.3</td>
</tr>
</tbody>
</table>

RADIOLOGICAL FINDINGS
Left lower extremity duplex venous Doppler revealed the absence of deep vein thrombosis of the leg.

DIFFERENTIAL DIAGNOSES
1. Rattlesnake envenomation to left lower leg - per history
2. Compartment syndrome left lower leg-left leg - has swelling and pain out of proportion to exam despite pain medication, some alteration of sensation in left foot
3. Acute myonecrosis of left lower leg-secondary to rattlesnake bite
4. Deep vein thrombosis left lower leg-patient - complaining of severe left lower leg pain post rattlesnake envenomation and immobility
5. Acute cellulitis - has puncture wound with swelling and pain to the surrounding tissue
6. Thrombocytopenia - has lower than normal platelet count
7. Leukocytosis - has an elevated white blood cell count, most likely a stress response to bite
8. Coagulopathy - elevated bleeding times with low platelets
9. Anemia - has a low hemoglobin and hematocrit

WORKING DIAGNOSES

1. Rattlesnake envenomation of left lower leg
2. Acute compartment syndrome of left lower leg

PATHOPHYSIOLOGY

The pathophysiology associated with both rattlesnake envenomation and compartment syndromes are both simple and complicated at the same time. Rattlesnakes belong to the pit viper family of snakes which have a poison which is considered hemotoxic. This venom consists of enzymes and proteins that cause localized necrosis and hemolysis.

The venom of rattlesnakes is intended for prey and not for humans. Rattlesnake venom is used by the animal for both lethality and digestive purposes. The venom is composed of a compound of polypeptides which induces hypovolemia in the snake’s prey by inducing damage to the endothelial cells, thereby allowing extravasation of blood and plasma into surrounding tissue. The same process in humans causes increased capillary permeability and myonecrosis. The venom is also known for the fibrinolytic property of an enzymatic glycoprotein that specifically targets the patient’s endogenous fibrin without activating the usual cascade of activated factor XIII.

Diagnosis of snakebite is based on clinical assessment and patient history. The most important factor determining the use of antivenom is by grading the severity of the envenomation present. (Table 2) The score was developed on a scale of 0 to IV; taking into account the factors of localized findings along with systemic findings. The higher the grade given by the clinician on assessment, the higher the risk of systemic findings and complications. This patient was given a score of III in the ED and was treated accordingly.

Compartment syndrome is a limb-threatening condition that rarely occurs after snakebites and should be considered after the administration of at least 20 vials of antivenom. At the most basic level, compartment syndrome is a result of edema in a closed and non-elastic muscle compartment which is surrounded by fascia and bone. After rattlesnake envenomation, a cascade of extravasation occurs, filling the site of the bite with electrolytes, albumin, and red blood cells.

Compartment syndrome arises due to a vicious cycle of edema causing hypoxia and acidosis which further increases capillary permeability and fluid extravasation. The edema is a result of volume increase in a closed fascial compartment, which ultimately can lead to a compromise of circulation as well as irreversible muscle injury and nerve conduction impairment. Tissue perfusion is maintained by the proportional difference between the capillary perfusion pressure of the tissue and the interstitial fluid pressures which is normally maintained within 20 mmHg of the diastolic pressure of the patient. For diagnostic purposes, a pressure that is within 30 mmHg of the diastolic pressure of the patient is indicative of compartment syndrome leading to a resulting muscle necrosis. This rise of the compartment syndrome, in relation to the diastolic blood pressure, is known as delta p. The use of this measurement has been shown to consistently indicate the presence of compartment syndrome.
syndrome than the individual compartment pressure measurement alone.\textsuperscript{14}

Muscle necrosis begins within 3 hours of the onset of compartment syndrome and irreversible damage occurs within 5 to 6 hours of onset.\textsuperscript{9} In the lower leg four fascial compartments exist, with the anterior compartment being the most frequently involved.\textsuperscript{11} These compartments of the lower extremity are at higher risk because of the re-profusion syndrome associated with vascular injuries in that part of the body. This mechanism is due to both the ischemic muscle injury and the dependent nature of the lower extremity.\textsuperscript{15}

**DIAGNOSTICS**

Compartment syndrome is a diagnosis made by clinical assessment. Traditionally, the seven P’s of compartment syndromes are cited as pain, pallor, parasthesia, paresis, poikilothermia, pressure, and pulselessness.\textsuperscript{13} The cardinal sign of compartment syndrome development is pain out of proportion to the patient’s clinical presentation.\textsuperscript{16} The most difficult aspect of diagnosing compartment syndrome with rattlesnake envenomation is differentiating between the presence of the condition and the findings that are consistent with severe envenomation. The similar findings of envenomation often mimic those of compartment syndrome; marked pain, swelling, tenderness, pain on passive stretch, and tenderness.\textsuperscript{17} Assessment of sensory and motor changes related to developing compartment syndrome should be related to the underlying nerve located within each compartment and its sensory territory distally.\textsuperscript{18}

With the close similarity in presentation, close assessment and the use of intra-compartment measurement should be used to assist with the diagnosis. The current recommendations are the measurement of compartment pressures with a commercially available device, although no differences have been found between the continuous monitors and the single use types.\textsuperscript{9} The biggest issue found with these devices is that only one compartment can be measured at a time, so a more feasible option such as serial exams have been found to be more sensitive for changes consistent with this diagnosis.\textsuperscript{9}

Laboratory and radiological studies are of no assistance in the determination of the presence of compartment syndrome. Instead, laboratory and radiological studies may be of use in ruling out other conditions that are known to be contributory or mimic this condition such as deep vein thrombosis and coagulopathies.\textsuperscript{19} Some of the laboratory tests that should be considered are serial creatine kinase (CK) levels to assess muscle damage, renal function tests such as blood urea nitrogen (BUN) and creatinine, monitoring of electrolytes such as potassium, coagulation panels (PT, PTT, INR) for monitoring of coagulopathies, and a complete blood count (CBC) for monitoring of anemia.\textsuperscript{5} An important radiological study to consider is a lower extremity venous Doppler to assess for the presence of deep vein thrombosis.

**PHARMACOLOGICAL INTERVENTIONS**

No pharmacological interventions are indicated for the treatment of compartment syndrome. However, pharmacological interventions are indicated for the treatment of rattlesnake envenomation that will reduce the likelihood of the development of this condition. This medication is the antivenom known as CroFab.

CroFab is ovine-derived antivenom that is specific for the treatment of snakebites from the Crotalidae family of snakes. The amount of CroFab that is given to each patient is based on the previously mentioned envenomation scale. This scale requires clinicians to accurately assess a wound and then use the score as a guide for the recommended amount of antivenom. (Table 3) The clinician must first assess the risks and benefits of the use of antivenom by understanding that the coagulation changes of envenomation is quickly reversible by administration, but the localized tissue damage of the bite does not reverse quickly.\textsuperscript{20} After the risks and benefits are assessed and establishment of the degree of envenomation by the practitioner have been determined, then administration is warranted. The scoring scale can be used in assessing the efficacy of the antivenom.

**Figure 3**

Table 3 Treatment of Snake Bites Based on Severity

<table>
<thead>
<tr>
<th>Grade</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Local wound care only; no antivenom required</td>
</tr>
<tr>
<td>I</td>
<td>Administration of about 5 vials of antivenom if necessary*</td>
</tr>
<tr>
<td>II</td>
<td>Administration of 5-15 vials of antivenom may be necessary</td>
</tr>
<tr>
<td>III</td>
<td>Administration of at least 5-15 vials of antivenom may be necessary</td>
</tr>
<tr>
<td>IV</td>
<td>Administration of at least 25 vials of antivenom</td>
</tr>
</tbody>
</table>

* Grade I copperhead bites usually not treated

The administration of the antivenom is to be used early in the therapy of snakebites to eliminate or lessen both the local
and systemic effects. The antivenom will actively bind with the venom components to prevent hypotension and coagulopathies and prevent the local manifestations such as myonecrosis. What is unknown is whether or not early use of antivenom actually reduces the incidence of compartment syndromes in humans, but does show promise in animal data and case reports. In the case of this patient, he was originally classified as III on the envenomation score and received a total of 20 vials of CroFab while in the ED. However, the patient’s pain and swelling continued to progress. The patient’s laboratory findings did improve from a coagulopathy standpoint after the administration of antivenom.

NON-PHARMACOLOGICAL INTERVENTIONS
Fasciotomies were once advocated as an early and appropriate intervention for all envenomations, but are now reserved for only those cases where compartment syndrome is either confirmed or suspected. The use of fasciotomy has still not been proven in human models as an effective treatment alone for the management of this condition. Animal models have demonstrated the only statistically significant improvement in myonecrosis is the use of the fasciotomy technique early in the treatment. The procedure should only be performed by specially trained surgeons and at a facility which has the resources to manage the patient postoperatively. This patient had a fasciotomy performed after the assessment by both the general and orthopedic surgeons. During surgery the patient was found to have compartment syndrome of both the anterior and lateral compartments of the lower leg. In addition, a significant amount of myonecrosis of several muscles located in these compartments was discovered.

REFERRALS/FOLLOW UP
The patient was returned to general surgery services for further treatment. Rehabilitation can be initiated within three days of surgery. The rehabilitation is slow, but most patients will have full recovery of residual function by 3 to 4 months. Most long term morbidity revolves around loss of function, weakness, paresthesia, or skin discoloration. The performance of the fasciotomy significantly increases the patient’s course of treatment and may also be associated with disfiguring scars and the need for further cosmetic surgeries. This patient was sent to a rehabilitation hospital after a 12 day stay in the hospital. No further complications were associated with his stay in the hospital postoperatively.

EDUCATION
The education of this patient was based on two distinct different subjects. The first subject is based on the prevention of snakebites, which involves avoidance of snakes and the use of a common sense approach to not attempting to handle or capture snakes. The second subject involves teaching the patient about the prognosis of recovery from the fasciotomy. Education also includes ensuring that the patient understands the importance of follow up and rehabilitation, as well as the signs of changes that are significant for immediate follow up.

SUMMARY
This case is representative of the need for constant and vigilant monitoring that is required for rattlesnake envenomations. The patient had a potentially limb-threatening complication which required surgical intervention, despite the appropriate initial treatment he received in the ED. With the emergence of improved antivenom medications such as Cro Fab, the fasciotomy is no longer considered a mainstay of snakebite treatment, and should not be considered a substitute for medication. However, the use of fasciotomy may still be indicated in the presence of compartment syndrome even though the literature is unclear on the efficacy of this surgery. The use of “cold steel” to cure may be necessary in cases in which life or limb is potentially jeopardized. Unfortunately, the numbers of snakebites which require fasciotomies are low in number and clinicians often times must rely on case reports or animal studies to make difficult treatment decisions.

The role of the Advanced Practice Nurse (APN) is to be vigilant is assessing changes in the patient’s condition. When a change in the patient’s condition occurs, the APN must be familiar with all treatment options and intervene immediately. Once an option is selected, the APN’s role will be to educate the patient on the short and long-term risks and benefits of the particular treatment and follow-up on the patient’s progress post treatment.

References
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