ELEVATED COMPARTMENT PRESSURES FROM COPPERHEAD ENVENOMATION SUCCESSFULLY TREATED WITH ANTIVENIN

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Abstract—Background: Copperhead envenomation causes local soft tissue effects; however, associated compartment syndrome is rare. We report a case of a 17-month-old with significantly elevated compartment pressures successfully treated with antivenin and supportive care. Case Report: A 17-month-old girl sustained a copperhead bite to the foot and presented with circumferential edema, erythema, and ecchymosis of the foot and distal ankle. The patient had palpable pulses and was neurologically intact. Four vials of Crotalidae polyvalent immune Fab was initiated and additional doses were administered in an attempt to achieve local control. Within 10 h of presentation, the patient’s edema extended to the groin, although sensation was maintained and pulses were documented by Doppler. Lower-extremity compartment pressures were measured and were most notable for an anterior pressure of 85 mm Hg, despite having received 12 vials of antivenin. Fasciotomy was deferred and the patient received two additional six-vial doses of antivenin to achieve local control. Compartment pressures improved with a 2.2-cm mean decrease in limb diameter within 48 h. Maintenance dosing was initiated and the patient ultimately received a total of 26 vials of antivenin. The patient did not develop significant coagulopathy or thrombocytopenia. Swelling continued to improve with return of limb function. Conclusion: In this case, early and aggressive treatment with antivenin may have avoided invasive fasciotomy, and its use should be considered in patients with copperhead envenomation and significantly elevated compartment pressures. © 2014 Elsevier Inc.

Keywords—copperhead envenomation; compartment syndrome; antivenin

INTRODUCTION

Crotalinae venom contains a complex mixture of proteins, peptides, lipids, biogenic amines, and metalloproteins that can cause profound local soft tissue effects (1). Swelling is usually confined to the subcutaneous tissue as the fangs rarely penetrate into the subfascial compartment. Despite significant soft tissue symptoms, compartment syndrome after Crotalinae envenomation is uncommon. Additionally, elevated compartment pressures may occur without clinical evidence of tissue hypoperfusion or neurovascular compromise (1–3). Although rarely appropriate for snakebites, fasciotomy has been the traditional approach to compartment syndrome; however, many of the existing surgical data predate the availability of effective antivenin. Animal models have demonstrated that antivenin decreases compartment pressures and can improve tissue perfusion (1). Elevated compartment pressures due to snake envenomation have been treated nonsurgically with antivenin; however, the majority of cases involve rattlesnake envenomation (2,3). We report a case of a 17-month-old with significantly elevated lower-extremity compartment pressures from a copperhead...
(Agkistrodon contortrix) bite successfully treated with antivenin and supportive care.

CASE REPORT

A 17-month-old previously healthy girl sustained a copperhead bite to the dorsum of the foot while playing in the family garage. The snake was identified by local Emergency Medical Services, who immediately transported the patient to the nearest Emergency Department (ED). The limb was immobilized during transportation, but other field treatment was deferred. Upon arrival, the patient had circumferential edema, erythema, and ecchymosis of the foot with extension to the distal ankle (Figure 1). Two puncture wounds were noted on the dorsum of the foot. Upon presentation, her range of motion was largely limited by severe pain and edema, yet she maintained a palpable dorsalis pedis pulse, and distal sensation was intact. Her initial laboratory studies were notable for prothrombin time 11.4 s, partial thromboplastin time 25.4 s, international normalized ratio 1.1, fibrin degradation products < 5 μg/mL, creatinine phosphokinase 230 IU/L, and platelets 310,000/μL. Due to the significant soft tissue effects, the child received an initial dose of four vials of Crotaline polyvalent immune Fab in the presenting ED and was subsequently transferred to a facility with a pediatric intensive care unit for further monitoring.

Upon arrival to the intensive care unit, the patient received another two vials of antivenin, yet the swelling progressed to the groin area with preserved neurovascular function. As a result, six additional vials of antivenin were administered. Despite these measures, the edema reached the inguinal fold with a precipitous increase in pain medication requirements. Orthopedic Surgery was consulted and a pediatric orthopedic surgeon measured compartment pressures with a Stryker needle using standard procedure. The compartment pressures of the lower extremity were measured as follows: anterior 85 mm Hg, lateral 55 mm Hg, posterior 27 mm Hg, deep posterior 34 mm Hg, foot 60 mm Hg, and quadriceps 30 mm Hg. At that time, distal pulses were measurable by Doppler, the patient had brisk capillary refill, and had intact pain and temperature sensation, although range of motion was limited secondary to pain and swelling. After a review of the available literature, and with consultation between the pediatric intensive care team, Orthopedic Surgery, and the poison center, the decision was made to defer fasciotomy and try additional antivenin, and another six-vial dose was administered. The swelling began to recede, with repeat compartment pressures 2 h after the fourth dose measured as: anterior 54 mm Hg, lateral 30 mm Hg (Figure 2). Based on the improved, though still elevated, pressures, another six-vial dose was given. Further clinical improvement was quickly noted, with progressively normalizing limb circumferences and decreasing pain medication requirement. The patient received one subsequent dose of two vials at 34 h, for a total dose of 26 vials over a 36-h time period. There was a 2.2-cm mean decrease in limb diameter within 48 h of the first pressure measurement (Table 1). The patient did not develop thrombocytopenia or coagulopathy. She was discharged on hospital day 4, and was ambulatory at that time. Two weeks after discharge, the child had full range of motion of the affected extremity, palpable pulses, with equal strength and no documented sensory deficits. There was complete resolution of skin changes, with approximately equal limb circumference, and the child was at her baseline level of activity.

DISCUSSION

Compartment syndrome is characterized by an increase in intra-compartmental pressure, with subsequent neurovascular compromise and tissue necrosis. Normal compartment pressures are generally below 15 mm Hg. Diagnosis is based on clinical findings and measurement of compartment pressures. Compartment pressures > 30 mm Hg are generally treated surgically with fasciotomy;
however, most of the surgical data are based on compartment syndrome due to causes other than envenomation, such as fracture or hemorrhage (4).

Compartment syndrome and increased intracompartmental pressures without evidence of neurovascular compromise are rare complications of copperhead envenomation. In one case series, there were no documented cases of compartment syndrome (5). In another, four fasciotomies were performed without documented compartment pressure measurements (6). Rattlesnake envenomation is more likely to lead to severe local reactions and compartment syndrome because rattlesnakes have larger fangs and more potent venom. Elevated compartment pressures ranging from 30 mm Hg to 80 mm Hg have been documented in rattlesnake envenomations (1). Risk factors for increased intra-compartmental pressures after a snake bite have also been identified and include envenomations in small children, involvement of the digits, the application of ice or cold packs, and delayed or inadequate antivenin administration (1).

Fasciotomy has been the traditional approach to compartment syndrome. The procedure involves incision of the skin and fascia to release the elevated pressures in the fascial compartment that can lead to neurovascular compromise (4). The downside to fasciotomy is that it is an invasive procedure with significant morbidity including scarring, contractures, infection, and even amputation (1,7). Additionally, there are few data to support the efficacy of this procedure when Crotalidae polyvalent immune Fab (CroFab; BTG International Inc., West Conshohocken, PA) is available (1). Crotalidae polyvalent immune Fab is a sheep-derived antivenin created from the venom of the following species: Crotalus atrox (western diamondback rattlesnake), C. adamanteus (eastern diamondback rattlesnake), C. scutulatus (Mojave rattlesnake), and Agkistrodon piscivorus (cottonmouth or water moccasin). Although copperhead venom is not used to produce Crotalidae polyvalent immune Fab, this product has been successfully used to treat copperhead envenomations. The major advantage of the sheep-derived product is that it has a lower incidence of infusion reactions and serum sickness compared to the traditional equine antivenin (8,9). Data regarding the use of Crotalidae polyvalent immune Fab to treat elevated compartment pressures are limited to a handful of case reports, primarily involving rattlesnake envenomation. In one rattlesnake envenomation, antivenin was administered in conjunction with hyperbaric oxygen and mannitol (1). Multiple doses of antivenin may be required, but are generally well tolerated, even in children. Of note, the pediatric dose for antivenin is the same as the adult dose, which can occasionally present challenges with large infusion volumes (9–12).

Animal studies have consistently demonstrated that muscle necrosis is caused by the effects of venom independent of the fascia. As such, elevated compartment pressures may be noted if the pressure is measured in the necrotic muscle (1). The utility of fasciotomy in the setting of snake envenomation may be limited because removal of the surrounding fascia does not affect the muscle necrosis caused by the venom. On the other hand, animal studies have shown that antivenom improves tissue perfusion and decreases elevated compartment pressures (13,14).

The patient presented in this case had significantly elevated compartment pressures and soft tissue swelling that improved after aggressive antivenin administration; however, the magnitude of effect of the antivenin in this case is unclear, as there was a significant delay in achieving local control of symptoms. Crotalidae antivenin has been shown to rapidly halt the progression of local soft tissue effects secondary to copperhead envenomation in as little as 4 h; however, delayed swelling and coagulopathy can occur despite treatment (8). As such, the true magnitude of the antivenin’s effect is difficult to quantitate. In this case, the patient’s improvement could also have been attributed to good supportive care and simply, resolution over time as the

Figure 2. Lower extremity approximately 22 h after presentation. The punctate marks on the skin are from a surgical pen that marked the area where the compartment pressures were measured.
venom was cleared. Although mortality from copperhead envenomation is rare, prolonged limb dysfunction ranging up to 1 year (median 6 weeks) has been reported in a case series where the majority of patients did not receive antivenin (5).

CONCLUSION

This case adds to the growing body of evidence that antivenin and supportive care without fasciotomy is an option for the treatment of envenomations with elevated compartment pressures but without neurovascular compromise. Animal data and human case reports suggest that early and aggressive antivenin therapy may prevent progression to compartment syndrome in patients with significant soft tissue findings and elevated compartment pressures, although further study is needed.

REFERENCES


Table 1. Timeline of Limb Circumference, Antivenin Administration, and Compartment Pressures

<table>
<thead>
<tr>
<th>Hours Post-exposure</th>
<th>Groin Circumference (cm)</th>
<th>Thigh Circumference (cm)</th>
<th>Calf Circumference (cm)</th>
<th>Foot Circumference (cm)</th>
<th>CroFab Dose (vials)</th>
<th>Compartment Pressures (mm Hg)</th>
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Ant = anterior; lat = lateral.
* Denotes time compartment pressure measured.