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The Role of Point-of-Care Ultrasound (POCUS) in Envenomation by a Desert Viper

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Patient: Male, 53-year-old
Final Diagnosis: Snakebite envenomation
Symptoms: Pain • swelling
Medication: —
Clinical Procedure: Antivenom administration • Point of care ultrasound (POCUS)
Specialty: Critical Care Medicine • Radiology • Toxicology

Objective: Challenging differential diagnosis

Background: There are few reports of crotaline envenomation in Qatar, where clinically significant snakebite is infrequently encountered. This report presents a case that resulted in significant hematotoxicity. The report introduces the concept that there may be a role for point-of-care ultrasound (POCUS) as an Emergency Department (ED) bedside imaging tool in the early evaluation of crotaline snakebites.

Case Report: A 53-year-old Bangladeshi male without any prior medical history or allergies presented to the ED at the Hamad General Hospital stating that a sand-colored snake with a large head had bitten him on an uncovered part of his distal right leg leading to moderate swelling. Baseline laboratory testing showed a single laboratory suggestion of hematotoxicity (borderline elevation in prothrombin time) and moderately elevated lactate, indicating the potential for localized tissue destruction. POCUS demonstration of subcutaneous edema extending proximal to the knee was interpreted as suggesting the bite may be sufficiently serious to warrant administration of antivenom as the swelling crosses a major joint.

Conclusions: The presentation of the current case provides useful information for crotaline envenomation evaluation and management in Qatar and surrounding Middle Eastern countries. The mainstays of therapy are early suspicion of hematotoxicity, close observation for soft tissue, and timely treatment with appropriate antivenom. The case presented also provides a suggestion that ED ultrasound (POCUS) may be of assistance in assessing and predicting subcutaneous edema extent in patients with crotaline envenomation.

MeSH Keywords: Snake Bites • Ultrasonography • Viper Venoms

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Background

Crotaline envenomation is a common worldwide occurrence, but there are few reports of such envenomation in the State of Qatar where clinically significant snakebite is infrequently encountered. Qatari snake species are similar to those found in the neighboring Middle East region, and the country uses crotaline antivenom that is produced for use in Saudi Arabia [1]. The point-of-care ultrasound (POCUS) has been previously reported to be of potential use in snakebites that involve tissue destruction. Emergency ultrasound has been found to be of use to demonstrate both superficial structural involvement and sparing of deeper muscle and tissues in patients with subcutaneous edema after crotaline snakebite [2].

This report outlines a case of envenomation that presented initially with minimal symptoms but ultimately was characterized by significant hematotoxicity. Early POCUS findings demonstrated edema that was far proximal to the area of clinically apparent swelling and tenderness. Though previously reported as a tool to identify the presence or absence of edema, POCUS application as a predictor of the spread of local tissue

toxicity has received little attention. The aim of the current report is to describe the multidisciplinary management of crotaline snakebite in Qatar's major hospital and to introduce the possible applicability of POCUS as an early tool to indicate clinically unapparent tissue involvement distant from the site of envenomation.

Case Report

A 53-year-old Bangladeshi male without any prior medical history or allergies presented to the Emergency Department (ED) at the Hamad General Hospital (HGH) stating that at 2330, a sand-colored snake with a large head had bitten him on an uncovered part of his distal right leg. The snake subsequently escaped capture.

Triage assessment revealed one snakebite, located on the distal medial right lower extremity (Figure 1). The patient reported pain at the site of the bite and in the surrounding area. The Emergency Medicine (EM) physician noted mild swelling at the distal leg at and in the tissue surrounding the bite site.



Figure 1. Bite location proximal to the medial right ankle (A) with close-up photo (B) showing minimal local swelling (photos were taken 5 h postenvenomation). (A) Bite location at the medial distal right lower extremity. (B) Foot/distal extremity is at the down of the image.

Table 1. Baseline laboratory testing at the presentation and throughout the course of treatment.

	Normal range	Patient labs at presentation 3 h postvenomation	Patient labs at 10 h postvenomation	Patient labs 4 h postanti-venom administration	Patient labs before discharge
CBC					
WBC	(4–10)×10 ³ /μL	15.6	16.6	19.2	8.3
Hemoglobin	(13–17) g/dL	14.5	15.8	15.2	12.2
Platelets	(150–400)×10 ³ /μL	199	115	115	197
Electrolytes					
Sodium	(135–145) mmol/L	137	135	137	135
Potassium	(3.6–5.1) mmol/L	5	4	3.7	4.8
Chloride	(96–110) mmol/L	105	106	110	105
Renal panel					
Creatinine	(64–110) μmol/L	92	80	79	72
Urea	(3.0–9.20) mmol/L	5.35	5.7	5.2	5.6
Liver function					
AST	(5–34) U/L	23	34	39	20
ALT	(0–55) U/L	27	26	23	21
Total bilirubin	(3.4–20.5) μmol/L	7	18	20	14
Albumin	(35–50) g/L	42	39	30	36
Coagulation					
PT	(7.8–9.9) s	10.3	44.7 ↑	20.7	9.7
APTT	(25.3–33.8) s	18.6	35.1 ↑	41.7	29.8
INR	(0.8–1.0)	1.1	4 ↑	2	1
D-Dimer	(0.00–0.55) mg/L	–	>34.18	>34.18	–
Fibrinogen	(1.80–3.50) g/L	–	<0.07	<0.7	–
Lactic acid	(0.5–1.6)	3.7	2.9	–	–

CBC – complete blood count; WBC – white blood cells; AST – aspartate aminotransferase; ALT – alanine aminotransferase; PT – prothrombin time; APTT – activated partial thromboplastin time; INR – international normalized ratio.

There was no oozing at the site. The physician ordered intravenous (IV) paracetamol for pain and oral amoxicillin/clavulanate for antimicrobial prophylaxis. Tetanus toxoid was given. The patient was noted to have continuing normal vital signs, and he was comfortable, declining further pain medication. Baseline laboratory testing was sent (see Table 1).

Examination of the foot distal to the bite revealed bounding pulses and normal neurovascular assessment. Evaluation of the bite area revealed mild to moderate swelling and tenderness, mostly within a few centimeters of the bite but with lesser swelling and tenderness extending 5 to 6 cm from the bite

puncture site. There was no circumferential swelling and no tightness to any part of the thigh, leg, ankle, or foot. The area of swelling and tenderness did not extend proximally to the knee or distally to the foot.

POCUS was performed with a handheld device (SonoSite iViz™, Bothell, Washington), using a high-frequency linear transducer with musculoskeletal preset at a depth of 2 to 5 cm initially requested by the medical toxicology rounder to provide an assessment of the distal arterial pulses in the foot. Although the ease of identifying pulses rendered POCUS unnecessary for the initially intended application, bedside images of the right lower

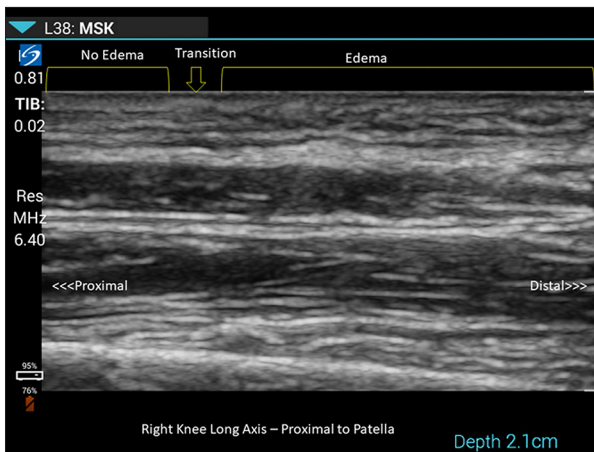


Figure 2. Point-of-care ultrasound of right thigh: demonstration of the transition zone from nonedematous thigh to area of subcutaneous edema (proximal end of the extremity is at the left of the figure).

extremity did prove useful in an unanticipated fashion. After the expected finding of localized subcutaneous edema in the immediate region of the bite, the probe was moved proximally in the right lower extremity and clearly demonstrated edema in the subcutaneous space proximal to the knee (Figure 2); POCUS identified this edema in an area that lacked any swelling or tenderness.

The EM's medical toxicology consulting service saw the patient at 0430, 5 h after the bite had occurred. The patient was shown a photograph (Figure 3) of a *Cerastes* desert viper, a crotaline snake that had been brought (dead) to the HGH ED the previous month by another patient. The current patient identified the snake that had bit him as looking nearly identical to the pictured snake.

The evaluation by the medical toxicology service was that the patient had a crotaline envenomation with only localized reaction, resolution of pain with minimal therapy, and a single laboratory suggestion of hematotoxicity (i.e., borderline elevation in prothrombin time [PT] with an unknown baseline). The patient had moderately elevated lactate, which seemed to indicate the potential for localized tissue destruction.

POCUS demonstration of subcutaneous edema extending proximal to the knee was interpreted as suggesting the bite may be sufficiently serious to warrant antivenom (using a guide indicating antivenom when swelling crosses a major joint) [2]. Given the absence of evidence on the use of POCUS to inform antivenom administration decisions, and given the lack of other definitive indications for antivenom therapy, a decision was made to follow the patient carefully and send a more detailed laboratory assessment (e.g., fibrinogen level) to inform decision making regarding antivenom.



Figure 3. Desert viper.

The patient was observed for 2–3 h while the laboratory workup proceeded. An X-ray of the bite site revealed no bony involvement or foreign body. The extended hematologic testing, which had been sent after the medical toxicology evaluation, indicated significant hematotoxicity. Most notable were low fibrinogen, thrombocytopenia, and a doubling in the PT (see Table 1).

Treatment

On the basis of the overall clinical picture, a decision was made to administer antivenom. The patient was moved to a higher-acuity area of the ED (to enable close observation during antivenom therapy). His leg was mildly elevated (to 15–20°) for comfort.

Antivenom administration

At approximately 10 h postenvenomation, infusion of four vials of antivenom diluted in 50 mL of normal saline was commenced at an infusion rate to deliver the medication slowly over an hour. The patient tolerated the initial half of the infusion well, but then developed hypotension (systolic blood

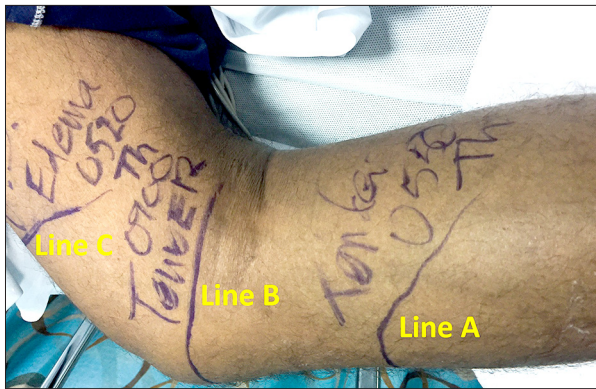


Figure 4. Skin markings on the right lower extremity (medial aspect) above and below the knee (the patient's foot is toward the figure's right side).

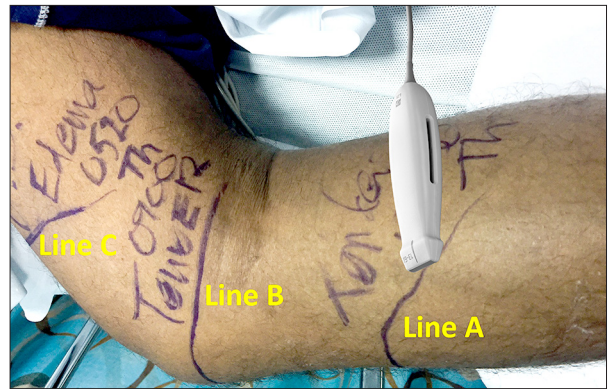


Figure 5. Demonstration of the ultrasound probe place and direction.

pressure drop to 65) with skin findings of diffuse wheals and urticaria. There were no respiratory issues other than mild tachypnea (the respiratory rate rose to 21).

The patient was diagnosed as experiencing either an anaphylactoid or anaphylactic reaction. The antivenom infusion was temporarily halted. Epinephrine (0.5 mg intramuscular [IM]) was administered immediately, followed by diphenhydramine (50 mg IM) and hydrocortisone (200 mg IV). The patient also received a fluid bolus (a total of 3 L of normal saline during the hours surrounding the anaphylactic/anaphylactoid reaction).

After the single episode of hypotension, the vital signs recovered. There was only a single episode of low blood pressure. There were never any voice changes or other signs of airway issues. There was no wheezing, and the patient's mental status remained unchanged. The infusion rate was slowed, and the patient's antivenom therapy was resumed.

Four units of fresh-frozen plasma (FFP) were administered, starting approximately 12 h after the initial patient presentation. The decision was made to admit the patient to the medical intensive care unit (MICU) for further monitoring and potential repeat antivenom therapy, as indicated.

A skin marker was used to indicate three lines over the course of the patient's ED stay (Figure 4). The first-timed line drawn at 0520 (line C in Figure 4) indicated the point at which subcutaneous edema was identified by POCUS (and POCUS only) approximately 6 h postvenomation. A second line (line A in Figure 4) depicts the proximal extent of tenderness identified on examination at 0550 (i.e., a half-hour before the marking of line C). A third line (line B in Figure 4) indicates that tenderness did not cross proximal to the knee-joint level until 0900 (Figure 5).

Outcome and follow-up

In the MICU, the patient remained hemodynamically and otherwise clinically stable with lab results trending as depicted in Table 1. Because of coagulopathy and a question of drowsiness, the MICU team requested a head computed tomography, which had normal results. The MICU team also administered antibiotics (piperacillin/tazobactam 4.5 g IV once with 5 days' prophylactic course of amoxicillin/clavulanate).

There were no repeat doses of antivenom administered. The patient was transfused with four units of FFP as the PT peaked at 44.7 (see Table 1).

The patient continued to have swelling and tenderness over the next 1–2 days, but there was no worsening of the right lower extremity findings. There were no signs of compartment syndrome. MICU and surgical consultants judged that compartment-pressure measurement risks outweighed the potential benefits (indications). The patient's swelling and tenderness began to resolve after approximately 36 h, and no compartment syndrome occurred. A formal ultrasound of the lower extremity was done to assess the vasculature; the results were normal.

The patient was transferred to a regular hospital bed approximately 2 days after the initial presentation to the ED. As shown in Table 1, the lab results corrected. The patient never developed any hematologic complications other than derangements in laboratory tests (i.e., there were no bleeding complications).

After 5 days in the hospital (including two in the MICU), the patient was cleared for discharge to a low-intensity unit near the hospital; this was a minimally monitored setting for patients with uncertain safety for discharge to home. He did not develop serum sickness during his stay in the hospital or in the low-intensity monitoring area where he remained for a further 5 days (total hospitalization period of 10 days) before discharge

home. He developed no complications during his stay in the low-intensity care setting.

Follow-up was obtained by telephone 1 month after the patient's discharge. He had no complaints and no recurrence of pain, swelling, or any complications potentially related to serum sickness or other sequelae of his snakebite.

Discussion

Snakebites in the Middle East

Both crotaline and elapid snake envenomations occur in the Middle East and surrounding countries [1,3]. Compared with the data available describing snake envenomations in many other parts of the world, there is a relative paucity of literature outlining the natural history and treatment of snakebite in Qatar. Anecdotally, snakebite in Qatar is quite unusual as a presenting complaint, with an average of one or two cases seen each year (in an ED with a monthly census of 40,000) [4].

Given the rarity of elapid envenomations in Qatar, the primary concern for snakebite cases in the country is crotaline envenomation. Although there are some worldwide reports of crotaline envenomation resulting in neurologic toxicity [5], neurotoxins have not been reported in Qatar, so the ED concerns focus on nonneurologic tissues (including blood).

The Saharan horned viper *Cerastes cerastes* shares some Qatari distribution with *Cerastes gasperetti* [1]. *Cerastes* snakes, or desert vipers, tend to be similar in appearance across related species; from an emergency treatment perspective, it is not necessary to differentiate between the species. The horned vipers are most notable for the eponymous supraorbital horn, although the horn may not be present in all such snakes. The characteristics of the snake in Figure 3 (e.g., large head, overall length up to 3 feet, dorsal markings with a white ventral surface, abrupt taper to a black tail) are suggestive of a *Cerastes* specimen. *Cerastes* are, in fact, the most familiar snakes of the deserts of North Africa and the Middle East stretching to Iraq, being responsible for many snakebites in humans [1].

The natural history of *Cerastes* envenomation tends to be non-fatal, with generally favorable outcomes attributable to early antivenom and avoidance of ineffective (and potentially harmful) interventions such as tourniquets [1]. Although a few fatal desert viper bites were seen in the 19th century French colonial military medical literature, there are few if any reports of death in recent years [6].

General care principles

In a patient such as this one in which there are limited and localized findings, there is no indication for compression bandages or other interventions that could worsen distal edema and compartment pressures. In fact, blockage of venous drainage can promote deep vein thrombosis and subsequent pulmonary embolism [6]. Similar recommendations against other early interventions (e.g., incising the bite area, extracting venom) are found in standard texts [6].

The crotalines that are encountered in Qatar are not associated with neurotoxicity seen with some other crotalines (e.g., Mohave rattlesnakes in the United States). To the authors' knowledge, airway and breathing support have never been needed for crotaline envenomation in Qatar.

Circulatory support with crotaline envenomation in Qatar follows the principles of snakebite therapy elsewhere. Unless hemorrhagic complications require volume support, or unless patients have volume depletion from another source (e.g., decreased oral intake, exposure to hot environment), electrolyte-balanced maintenance therapy should suffice. The patient's IV fluid administration in the HGH ED was not necessary because of massive hemorrhage; it was rather aimed at assisting hypotension treatment (i.e., using the Frank-Starling principle). Overzealous fluid administration carries the same risk of hemodilution (including clotting-factor dilution) in snakebite cases as it carries with other patients.

Antivenom use in Qatar

The antivenom used in Qatar is obtained via hyperimmunization of Arabian horses to venoms from *Bitis arietans*, *Echis coloratus*, *Echis carinatus*, *Naja haje*, *Walterinesia aegyptia*, and – with the most relevance to the current case – *C. cerastes*. The use of horses to generate snake-related antivenom is the most common approach in Asia. However, there is investigational evidence that dromedary camel-related antivenom production may be equally efficacious (and fiscally preferable), at least for the *Echis* species [7].

There are general rules guiding the decision to use antivenom. For crotaline envenomation, antivenom is recommended when there is profound derangement of coagulation, significant bleeding or hemodynamic complication, or spread of swelling and tenderness beyond the local site (particularly if such findings cross a major joint such as the ankle or knee) [6].

Compartment syndrome in the extremities (and even in the abdominal compartment) can develop after crotaline envenomation [8–10]. Of particular relevance to Qatar, a 2017 report from neighboring Saudi Arabia found an incidence of

compartment syndrome of just over 3% [11]. Thus, attention needs to be paid to compartment pressures with careful assessment of neurovascular status. POCUS may be helpful in these cases (e.g., to demonstrate distal pulses), but the difficulty in differentiating crotaline venom-mediated tissue toxicity from compartment pressure-mediated findings often translates into a need for the use of a direct transducer system such as the Stryker device (Stryker Corporation, Kalamazoo, Michigan).

The difficulty of differentiating venom effects from early compartment syndrome can lead to delayed diagnosis and unsalvageable tissue [8,12]. Patients should be warned that fasciotomy will not necessarily save necrotic muscle after envenomation, and fasciotomy should probably not be undertaken until coagulation parameters are restored [6]. The complexity of issues surrounding compartment-pressure assessment and surgical intervention is such that multidisciplinary medical/surgical discussion (as occurred in this case) is recommended.

Ultrasound in snakebite

Early ED-focused ultrasound texts included cellulitis and associated edema findings as important applications of POCUS [13]. The finding of transversely oriented subcutaneous hypoechoic edema with reticular extensions is nonspecific but informative. In the current case, POCUS was initially requested for its more traditional application of assessing for pulses in the foot distal to the bite. On physical examination, the dorsalis pedis and posterior tibial pulses were easily identifiable without the need for sonographic imaging. Since the ultrasound machine was present, it was applied to the entire involved lower extremity to assess the extent of edema.

This case's initial POCUS finding was unexpected in terms of its location in an anatomic area, indicating tissue involvement that was not apparent to examining physicians. Despite the tissue involvement's demarcation line (based on the patient query and physical examination) being limited to within approximately 10 cm of the bite site, POCUS delineated obvious edema at least twice as far away from the bite site. With the bite site in this patient being located just proximal to the right ankle, POCUS identified a well-delineated edema margin above the knee. This area, which was not clinically swollen, nonpainful to the patient, and nontender, was only identified as abnormal on POCUS at the time of the imaging examination (about 6 h postbite). Within a few hours, though, the patient's clinically detectable tissue involvement had spread to involve the high level where there was swelling, pain, and tenderness.

No clinical decision making was based on the POCUS findings in this patient's case. One instance of POCUS-demarcated edema

that seemed to predict ultimate tissue involvement was – and is – insufficient to drive clinical decisions. However, the suggestion that POCUS can assist in early identification of tissue involvement that is otherwise occult seems worth further study. If (and only if) further analyses confirm that POCUS-identified levels of edema are predictive of overt tissue involvement in crotaline envenomation, then POCUS could be a useful tool for triaging snakebite cases and even guiding earlier administration of antivenom.

POCUS has been previously reported to be of potential use in snakebites that involve tissue destruction. In California, ED ultrasound has been found to be of use to demonstrate both superficial structural involvement and sparing of deeper muscle and tissues in patients with subcutaneous edema after crotaline snakebite [2]. In South Africa, POCUS was found to be useful in depicting the degree of edema in snake-bitten extremities as compared with contralateral normal extremities [14]. In neither of these reports was there specific investigation as to whether POCUS was useful as a predictor of the ultimate level of tissue involvement. We demonstrate in our case that the role of ultrasound in snake bite can be extended to assess the tissue destruction and early detection of edema and its extent, which help in prompt decision making and further management.

Conclusions

It is hoped that the presentation of the current case can provide useful information for crotaline envenomation evaluation and management, particularly for snakebites occurring in Qatar and surrounding Middle Eastern countries. The mainstays of therapy are early suspicion of hematotoxicity, close observation for soft-tissue and coagulopathy complications, and timely treatment with appropriate antivenom. The case presented also provides a suggestion, but not conclusive evidence, that ED ultrasound (POCUS) may be of assistance in assessing and predicting subcutaneous edema extent in patients with crotaline envenomation. Further investigation of the role of POCUS in triaging crotaline envenomation is warranted.

Acknowledgements

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Conflict of interest

None.

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