


## CASE REPORT

# Massive cutaneous complications due to snakebite: A case report and literature review

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## Abstract

Wound infections due to snake bites such as cellulitis and necrotizing fasciitis, although not common, are seen in snake bites and if left untreated can cause serious complications.

## KEYWORDS

antivenom, hemorrhagic blisters, snakebite

## 1 | INTRODUCTION

Wound infections due to snakebite such as hemorrhagic blisters and cellulitis, although not common, if untreated can cause serious complications. We present a 65-year-old man with massive cutaneous complications due to a snakebite. We recommend that wound infections should be considered as differential diagnosis in snakebite management.

Snakebite is a common and very important issue threatening health in different parts of the world, including Iran.<sup>1</sup> The clinical manifestations of snakebites are varying and depend on many factors, including the species of snake, the amount and strength of the venom injected, the location of the bite, and the patient's own factors, such as age, the underlying disease.<sup>2</sup>

Wound infections following snakebites such as cellulitis and necrotizing fasciitis, although not common,<sup>3-5</sup> are seen in the bites of snakes and if untreated can cause serious

complications such as necrotizing fasciitis, extensive local tissue damage, and progressive sepsis that can be associated with acute renal failure (ARF), thrombocytopenia, and coagulopathy<sup>2</sup>; although standard antivenom treatment can reduce the toxic hemorrhagic or neurotoxic effects of venom,<sup>6-8</sup> the progression of compartment syndrome and bacterial tissue infection cannot be prevented by antivenom therapy<sup>9,10</sup> and requires emergency surgical procedures such as fasciotomy or amputation and broad-spectrum antibiotics and hospitalization in the intensive care unit.<sup>3,7,11,12</sup>

On the other hand, in some cases of snakebites, the patient does not notice the bite and after a while suffers from local symptoms and sometimes systemic complications that if not diagnosed and treated in time can lead to massive complications and injuries that will complicate the treatment. Thus, we describe a rare case of wound infection with hemorrhagic and nonhemorrhagic blisters following snakebite.

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## 2 | CASE PRESENTATION

A 65-year-old man was referred to the Cardiovascular Center following chest pain with dissemination to the left upper extremity, cold sweats, chills, who had nausea and vomiting, and edema in the left upper extremity. At the time of entering this center, the patient had no fever and blood pressure was 113/68 mmHg, pulse rate was 76 beats/min and respiratory rate was 20 breaths/min. In examination, the ECG had a normal sinus rhythm and showed no changes indicative of myocardial infarction. Blood samples were also taken to test for cardiac enzymes, Troponin  $<0.2$  and BUN =46 mg/dL and Creatinine =2.5 mg/dL. After 6 hours, the swelling of the left upper limb progressed and multiple blisters appeared, after which the patient was referred to an infectious center in northern Iran for examination for infection, necrotizing fasciitis, and compartment syndrome. After admission to the infectious center, the patient had a fever ( $T = 38.5$ ) and tachycardia ( $PR = 108/\text{min}$ ) with a decreased level of consciousness. In the emergency room, at first the patient's airway was checked out and to monitor his vital signs, cardiac monitoring and pulse oximetry along with oxygen therapy with  $O_2$  mask were performed. Blood pressure and respiratory rate were within normal limits, and examination of the lungs, abdomen, and central nervous system showed no abnormal findings. On examination of the left upper limb; there was erythema, warmth, stiffness, nonpitting edema, and limitation of active movement. Also, vesiculobullous lesions were seen on the dorsal surface of the hand to the wrist and both

flexor and extensor surfaces of the forearm and arm up to the proximal arm and left axillary area (Figure 1A, B).

The location and size of the axillary lymph nodes were in normal range and the left radial pulse was weakly palpable. Also, swelling, redness, and localized infection were seen in the distal third finger of the left hand. According to the patient's history of the burning, redness, and blisters on the distal third finger of the left hand after lifting a heavy object within 3 days ago and also living in a rural district despite having venomous snakes, he was hospitalized with diagnosis of snakebite in the poisoning ward.

The patient had no history of smoking or drug usage, he had a history of dyslipidemia, hypertension, diabetes mellitus, and ischemic heart disease, which had been controlled with appropriate medications and was asymptomatic in routine life. He also had no history of asthma, allergies, rhinitis, dermatitis, or eczema and did not have a history of similar bites in the past.

In the primary tests performed, BUN and Creatinine increased compared to the measured values in the Heart Center, there was also a decrease in platelet count and a prolongation of PT and PTT, but the patient had no evidence of hemorrhage and coagulopathy, and liver enzymes were within the normal range; also, color Doppler ultrasound of the arteries and veins of the left upper extremity did not provide evidence of thrombosis. The ultrasound also showed multiple fluid-containing tracts, and according to surgical and orthopedic consultation, there was no evidence of necrotizing fasciitis or compartment syndrome.



**FIGURE 1** Vesiculobullous lesions before treatment (A and B) and after treatment (C and D)

On the first day of hospitalization, with the possibility of viral infection, patient was prescribed acyclovir tablet 400 mg Tds, and for bacterial infection, ceftriaxone vial 1 gr Bd, teicoplanin (Targocid) 400 mg Bd and meropenem 1 gr Bd intravenous infusion and as well as with probability of snakebite, 5 vials of antivenom (Hexavalent immune Fab is produced by inoculating horse plasma with the venom of Iranian Cobra and Viper snakes species; each vial contains 1 gram per 10 mL) via intravenous infusion, then 6 hours after the first injection, received 5 vials of antivenom and also 2 vials of antivenom every 6 hours in three times as a maintenance dose along with the medications he was already taking. The left upper limb was elevated, and a hot water bag was used to reduce stiffness and edema in blister-free areas.

As for the increase in BUN and creatinine in the patient's blood sample, nephrology consultation was requested. Also, following receiving antivenom, decrease in BUN and Creatinine levels and normalization of the level of consciousness, the diagnosis of acute interstitial nephritis (AIN) following a snakebite was proposed. On the second day, according to raising the BUN and creatinine in the patient's blood sample, teicoplanin (Targocid) antibiotic discontinued by the nephrologist, ciprofloxacin 200 mg IV infusion replaced and the dose of ceftriaxone (1 g Bd), meropenem (1 g Bd) was adjusted.

The wound was drained and then Eude Alibore solution (it contains zinc sulfate (1.5%), copper sulfate (0.5%) and camphor with antiseptic and local analgesic properties which it reduces skin inflammation), silver sulfadiazine, and zinc oxide ointments were also used for topical treatment of blisters.

The patient was monitored in the poisoning ward for 3 weeks, after which the fever, hematoma, and skin lesions resolved; the left hand edema appeared at the time of admission (July 26, 2019) and was completely resolved at the time of discharge (August 16, 2019), the radial pulse is fully and symmetrical in the involved limb. Also, serum levels of BUN, creatinine, PT, PTT, and INR returned to the normal range, and the patient was discharged from the hospital in a good general condition (Figure 1C, D).

### 3 | DISCUSSION

Most snakebites commonly produce local tissue edema and hematologic toxicity. Snake venom can simultaneously damage tissue, affect blood vessels and blood, and alter transmission at the neuromuscular junction. It is difficult to attribute specific pathology or pathophysiology to any particular component of snake venom. In fact, clinical manifestations often occur as the result of several venom components. For example, local tissue injury results from venom metalloproteinase, hyaluronidase, and phospholipase A2 (PLA2), which both

contribute to swelling through disruption of the extracellular matrix and basal membrane surrounding capillary endothelial cells.<sup>13</sup>

The venom effects on the hematologic system are very complex. Many components act as anticoagulants. Similarly, platelets may be inhibited, activated, agglutinated, aggregated, or inhibited from aggregating by various venom components. Venom components can be grouped according to the structure and enzymatic activity, but as noted above with local tissue damage, components within several groups may contribute to similar effects. Platelet effects result mainly from the action of disintegrins, although C-type lectin-like proteins (CLPs), PLA2 enzymes, and other proteins also have platelet-modulating effects. Specific hematologic effects are snake species dependent, with no single venom containing all of the identified hemostatically active components. Toxins of some snakes are the thrombin-like and fibrinolytic enzymes.<sup>14</sup>

Snake venom contains various toxins that acting systemically and locally, including, cardiotoxins, myotoxins, hemostasis toxins, neurotoxins, and renal toxins, that can cause the following disorders containing rhabdomyolysis, acute kidney injury, paralysis of the extremities, compartment syndrome, wound necrosis, coagulation disorder, persistent mydriasis and respiratory distress, cardiac dysrhythmia.<sup>15</sup>

Treatment by antivenom can reduce the envenomation effects on various systems (coagulation, central nervous system, cardiovascular, and gastrointestinal system); however, antivenom cannot reverse the effects of local tissue destruction or necrosis.<sup>13</sup> Sever wound infections, such as cellulitis and necrotizing fasciitis following venomous snakebites, are not common; they have been reported in up to 30.8% of patients after a snakebite and require aggressive treatment.<sup>3,4</sup>

The common signs and symptoms of wound infections and cellulitis, such as erythema, inflammation, warmth, and local pain, may develop in the early hours to days. However, the risk factors developing from cellulitis to necrotizing fasciitis secondary to a snakebite have seldom been investigated.<sup>15</sup>

One of the most important complications of snakebite with local envenoming is soft tissue infections. The snake venom with proteolytic properties causes extensive tissue destruction and devitalization, thus predisposing the wound to bacterial infection from the snake's indigenous oral flora. Although in patients with snakebite, bacteria are a major cause of wound infection, the role of prophylactic antibiotics to prevent their formation is discussible. However, the spectrum of bacteria from the venom and oral cavities of snakes vary with geographic area as well as with the species and the oral health of the snake, and these factors cannot easily be extrapolated to snakes in the rest of the world.<sup>16</sup>

In our patient after assessments and excluding the possibility of heart disease, infectious diseases, and compartment syndrome, due to the burning sensation in the tip of the third

finger of left upper limb after lifting a heavy object and the occurrence of hemorrhagic and nonhemorrhagic blisters in this limb with suspected snakebites, standard treatment with antivenom started for the patient and due to the rapid response with this treatment and the endemicity of the area in terms of snakebites, the diagnosis was definitive.

Hemorrhagic blisters often form at the site of the bite digits but may occur at any bite location or even in dependent areas distant from the bite. These blisters usually do not appear until hours after the bite. The tissue beneath these blisters is usually healthy, although large blisters can cause necrosis in their underlying tissue.<sup>2</sup>

Coagulopathy, thrombocytopenia, or a combination of the two may be present despite a paucity of other local or systemic effects. A decrease in platelet count, as well as decrease in fibrinogen with elevation of prothrombin time (PT), may be mild or moderate initially and may either remain so or continue to worsen for several days following the envenomation.<sup>2</sup> The standard antivenom treatment can reduce these toxic hemorrhagic and neurotoxic effects.<sup>6–8</sup> However, early usage of antivenom following a snakebite showed a trend toward a better local outcome within 12 hours. The prophylactic use of antibiotics was still controversial.<sup>7</sup>

## 4 | CONCLUSION

It should be noted that wound infections caused by snakebites if left untreated in a timely manner can lead to complications such as necrotizing fasciitis, compartment syndrome, or superimposed bacterial infection, which require hospitalization, the use of broad-spectrum antibiotics, and emergency surgical procedures; and since blisters usually do not appear until hours after the bite. Consequently, in patients who had topical edema and swelling along with hemorrhagic or nonhemorrhagic blisters with unknown causes, it is recommended that snakebite should be considered a differential diagnosis, particularly in areas where venomous snakes are frequently common.

## ACKNOWLEDGMENTS

Published with written consent of the patient.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

## AUTHOR CONTRIBUTIONS

ZZ: involved in interpretation and collecting of data, and editing the manuscript. LD and AZ: involved in drafting first version of manuscript and editing. MB and MS: involved in writing, editing, and preparing the final version of manuscript. MF: involved in critical revising. RT: is responsible

for collecting data and submitting the manuscript. All authors: reviewed the paper and approved the final version of the manuscript.

## INFORMED CONSENT

This study was conducted according to the declaration of Helsinki principles. Also, CARE guidelines and methodology have been followed in this study. Written consent for publication of this case report was obtained from the patient.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This research was reviewed and approved by the research ethics committee of Mazandaran University of Medical Sciences (IR.MAZUMS.REC.1399.134). The patient wrote the informed consent for participating in this study.

## DATA AVAILABILITY STATEMENT

The data are available with the corresponding author and can be achieved on request.

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**How to cite this article:** Sadeghi M, Barazandeh M, Zakariaei Z, et al. Massive cutaneous complications due to snakebite: A case report and literature review. *Clin Case Rep*. 2021;9e04129. <https://doi.org/10.1002/ccr3.4129>