

Recovery of Severe Envenomation with Delayed Antivenom Administration

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ABSTRACT

Up to our knowledge we are reporting the first case of delayed administration of antivenom followed by full recovery; a 25 year old male patient who was referred as disseminated intravascular coagulopathy (DIC) along with acute respiratory distress syndrome (ARDS). Severe envenomation with snake bite was highly suspected and antivenom was administered five days post envenomation, recovery achieved after second dose which was given six hours after first dose.

Key words: Antivenom, ARDS, DIC, Snake bite.

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Introduction

Snake bites are not rare in Jordan and can be fatal if untreated properly, there are 37 species of snakes in Jordan, seven of which are venomous, the commonest and most poisonous is Palestine viper (*Viperaepalaestinae*) and is a leading cause of snakebite within our region.⁽¹⁾

Some snake venoms contain hemotoxins that can result in widespread bleeding, disseminated intravascular coagulation (DIC) and death.⁽²⁾ Usually envenomation symptoms and signs shown 15-120 min after the bite ; venom dosage per bite depends on the elapsed time since the last bite, the degree of threat perceived by the snake, and size of the prey. Nostril pits respond to the heat emission of the prey, which may enable the snake to vary the amount of venom delivered.⁽³⁾

Antivenom is the only effective antidote for snake venom. The purpose of any antivenom is to bind the toxins in the venom and prevent both local and systemic results. The literature and the

manufacturers of the snake antivenom recommend administration within 6 hours to be repeated every 4 to 6 hours until definitive improvement.^(2,4) Up to our knowledge there are no reported cases for antivenom administration after five days.

Case Report

Hereby we are reporting a 25 year old male patient, soldier, not known to have any medical illness, presented with left ankle swelling to Emergency department. Patient recalls history of trauma (something hit his foot) one day prior to presentation, he had been evaluated by an orthopedic resident and was managed as ankle sprain, so he was discharged home with cast and nonsteroidal anti-inflammatory drugs (NSAIDs). Four days later he represented to a peripheral hospital with fever and chest symptoms and he was referred to our hospital upon family request. At arrival to our emergency department; his vital

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Table: patient parameters response to antivenom administration

	Zero time 1 st dose	6 hours 2 nd dose	24 hours	48 hours
Bl.p (mmHg)	80/30 (Dop)	100/50 (Dop)	120/70	120/70
I.N.R	5.4	4.3	2.0	1.4
Plat	20,000	50,000	100,000	170,000
CXR	ARDS	ARDS	Improved	Improved
O ₂ Sat (%)	80	90	96	96
FiO ₂	100	90	60	Extubated

Bl.p (blood pressure), I.N.R (International normalized ratio), Plat (platelets count), CXR (chest x-ray), O₂ Sat (Oxygen saturation)

signs were unstable with blood pressure of 90/40 mmHg, temperature was 38° C axillary, regular regular heart rate of 110/min, respiratory rate of 35/min and O₂ saturation of 91%. Chest examination revealed bibasilar crepitations. Other physical examination was unremarkable apart from a cast over left ankle, without evidence of edema or deep venous thrombosis. The patient was admitted to critical care unit and was started on supportive therapy along with broad spectrum antibiotics after sending septic work up. Investigations revealed leukocytosis with thrombocytopenia, renal impairment with prolonged PT and INR of 4.2, positive DIC screen. Chest x-ray showed bilateral infiltrate, arterial blood gases showed respiratory acidosis, the patient condition deteriorated demanding intubation. Our impression was that the patient is having DIC but there were no clear evidence of the cause of DIC, so decision was made to remove the cast and the big surprise was Fang marks, so a provisional diagnosis of snake bite with severe envenomation was made, the patient condition continues to deteriorate in spite of negative cultures to date so team decision was made to give anti-venom immunotherapy although the duration of the snake bite was at least 5 days; polyvalent snake antivenin PSA (Equine) was given as protocol: 40ml anti-venom was diluted in 5ml normal saline /kg body weight and infused slowly intravenously over a period of 60 minutes. Improvement started after first dose as shown in the table below; the patient condition parameters at zero time i.e. before starting antivenom immunotherapy and follow up after six hours when we gave him the second dose; the patient was hypotensive on dopamine infusion

with laboratory data of DIC and bilateral infiltration on chest x-ray. After 24 hours the patient managed to get off dopamine with improvement in platelets count and Oxygen saturation and he was successfully extubated after 48 hours with full recovery after 2nd dose. As shown in the table improvement started after first dose with full recovery after 2nd dose (six hours after first dose). Two days later he was transferred to the ward. Fortunately our patient did not develop anaphylaxis from the antivenom immunotherapy.

Discussion

Venomous snakes are classified into two important species, elapidae and viperidae. Elapidae have short, permanently erect fangs and include cobra, krait, coral snakes and sea snakes. While Viperidae have long fangs folded up against the upper jaw that erect when the snake strikes.

Venom is mostly water and its destructive properties mainly due the presence of enzymatic proteins like proteases, collagenase, and arginine ester hydrolase. Depending on the venom component the clinical picture varies from local tissue damage, coagulopathy, shock, neurotoxicity and renal toxicity.⁽³⁾

The most frequent site for snake bite is the lower extremity as in our patient and this is mostly due to easy accessibility and more contact with land.⁽⁵⁾

Antivenom therapy is the key to the medical management of snakebite; its neutralizing antibody gives antivenin efficacy. There are two kinds of antivenom available: 1st one derived from horse serum after the horse is injected with sublethal doses of snake venom this has been manufactured since 1956 but this one can be immunogenic because it does contain other serum proteins. The latest version (CroFab, Savage), is a monovalent immunoglobulin fragment derived from sheep but purified to avoid other antigenic proteins and this was approved by the US Food and Drug Administration (FDA) in 2000.

Grading envenomations is a dynamic process that is over several hours, an initially mild presentation may progress to a moderate or even severe reaction demanding antivenom administration. Grades are defined as mild, moderate, or severe.⁽⁵⁾

There is no available data regarding the efficacy of delayed administration of antivenom. Al-Hashaykeh *et al* ⁽⁶⁾ published a case of delayed administration of antivenom 3 days post envenomation.

One study from the southwest United States demonstrated a reduction in rate of fasciotomy after more liberal FabAV dosing. ⁽⁷⁾

Antivenom therapy can be associated with an immediate hypersensitivity reaction type I and serum sickness type-III, ⁽⁷⁾ mandating emergency treatment without discontinuation of the antivenom treatment.

Antivenom administration should be considered in patients with envenomations complicated by marked and progressive local signs, delayed systemic signs and laboratory abnormalities more than 24 h after envenomation despite administration of earlier dose.

Some case reports demonstrated that delayed administration of antivenom may be beneficial for patients with coagulopathies and local symptoms greater than six hours after envenomation. A case series by Lavonas *et al.* ⁽⁷⁾ reported 28 patients with severe envenomation, all with clinical improvement after optimal dosing beyond an 18-hour period.

As Geoffrey K Isbister *et al* ⁽⁸⁾ said although usually patients present with a report of a definite or highly suspected snakebite but few patients the suspicion confirmed when patients present after a collapse or seizure and investigations revealed coagulopathy with no report of a snakebite, as is the case in our patient when he recall a minor trauma and snake bite was only suspected after he had DIC and ARDS.

Carstairs *et al* ⁽⁹⁾ published a paper showing that Antivenom administration in an envenomated patients significantly increased platelets aggregation that will reverse the coagulopathy and this emphasized that even with delayed cases with coagulopathy secondary to envenomation will benefit from administration of antivenom immunotherapy.

Conclusion

Antivenom therapy is the key to the medical management of snakebite and ideally should be administered as early as possible. It can be lifesaving even in those presented late, so there should be no contraindication for delayed administration in life threatening condition.

References

1. **McDiarmid RW, Campbell JA, Touré T.** 1999. Snake Species of the World: A Taxonomic and Geographic Reference, Volume 1. Herpetologists' League. 511 pp.
2. **Gold BS, Dart RC, Barish RA.** Bites of venomous snakes. *N Engl J Med* 2002; 347(5):347-56
3. **Barlow A, Pook CE, Harrison RA, Wüster W.** Coevolution of diet and prey-specific venom activity supports the role of selection in snake venom evolution. *Proc Biol Sci* 2009; 276(1666):2443-9
4. **Rosen PB, Leiva JI, Ross CP.** Delayed antivenom treatment for a patient after envenomation by *Crotalus atrox*. *Ann Emerg Med* 2000; 35: 86-88.
5. **Sotelo N.** Review of treatment and complications in 79 children with rattlesnake bite. *Clin Pediatr (Phila)* Jun 2008; 47(5):483-9
6. **Al-Hashaykeh N, Al Jundi A, Abuhasna S.** Delayed administration of antivenin three days after snake bite saves a life. *Anaesth Pain & Intensive Care* 2011; 15(3)
7. **Bentur Y, Zveibel F, Adler M, Raikhlin B.** Delayed administration of *Vipera xanthina palaestinae* antivenin. *J Toxicol Clin Toxicol* 1997; 35(3):257-61
8. **Isbister GK.** Snake bite in Australia: a practical approach to diagnosis and treatment. *Med J* 2013; 199 (11): 763-768.
9. **Carstairs S.** Crotaline Fab antivenom reverses platelet dysfunction induced by *Crotalus scutulatus* venom: an in vitro study. *Acad Emerg Med* 2013; 20(5):522-5 (ISSN: 1553-2712)