CASE REPORT

Delayed administration of antivenin three days after snakebite saves a life

Nidal Al-Hashaykeh, MD*, Amer Al Jundi, BSc**, Said Abuhasna, MD***

** Pediatric Intensivist, ** Clinical Pharmacist, *** Chairman Department of Critical Care Medicine*
Tawam Hospital, Al Ain, (United Arab Emirates)

Correspondence: Said Abuhasna, MD, Chairman, Department of Critical Care Medicine, Tawam Hospital, PO Box 15258, Al Ain (United Arab Emirates); Tel: +971 3 707 4406; Fax: +971 3 707 4409; Email: sabuhasna@tawamhospital.ae

ABSTRACT

Snakebites can be deadly if not treated quickly. Some snake venoms contain hemotoxins that can result in widespread bleeding, disseminated intravascular coagulation (DIC) and a rapid death. This can be prevented by giving antivenom within hours, if not immediately. We report a case of a patient, who continued to deteriorate after 24 hours of envenomation, developed DIC and compartment syndrome within hours of the bite, in spite of the earlier treatment with polyvalent snake antivenin [PSA(Equine)]. The patient was then given a second dose of PSA (Equine) three days after envenomation which resulted correction of coagulopathy and complete improvement of the local symptoms.

Key words: Polyvalent snake antivenom; Snake bite; Compartment syndrome; DIC.
Citation: 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):167-169.

INTRODUCTION

Snakebites can be deadly if not treated quickly. Children are at higher risk of serious complications or death due to snakebites because of their smaller body size. Getting to an emergency room as quickly as possible is very important. If properly treated, many snakebites will not have any serious effects. The clinical features of the snakebites reflect the effects of the venom components. These include local tissue damage, ranging from swelling of the bitten limb to necrosis of the skin and muscle, abnormal blood clotting and bleeding, hypotension and shock, neurotoxicity that can lead to paralysis of respiratory muscles requiring assisted ventilation, and renal toxicity[1]. Symptoms and signs vary according to the species of snake involved in the bite and the amount of venom injected. Sometimes the identity of the biting snake can be confirmed by examining the dead snake; it may be strongly suspected from the patient's description or the circumstances of the bite or from knowledge of the clinical effects of the venom of that species. This information will enable the doctor to choose appropriate antivenom, anticipate the likely complications and therefore take appropriate action. If the biting species is unknown, recognition of the emerging pattern of symptoms, signs and results of laboratory tests (the clinical syndrome) may suggest which species was responsible.

A polyvalent equine antivenin is efficacious against both systemic and local manifestations if given within hours. A search on Medline did not reveal any data definitively demonstrating the efficacy of delayed administration of PSA in a case after 3-days of snakebite.

CASE REPORT

A 12 years old, previously healthy Emirati boy was admitted to a local hospital 30 minutes after having been bitten by a snake on the lower third of the anteromedial aspect of his left leg. The snake by description and based on the clinical syndrome was suggested to be sand viper (cerastes vipera). The patient received 5 ampoules (50 ml) of PSA, 65 mg of inj. hydrocortisone for anticipated anaphylaxis, and 3 units of fresh frozen plasma for anticipated DIC at the local hospital where the child first reported.

Despite active intervention, laboratory parameters revealed a state of DIC (elevated levels of prothrombin time (PT), activated partial thromboplastin time (PTT), INR and undetected fibrinogen). The patient developed compartment syndrome in his left leg 24 hours later. Since the local hospital was not well-equipped and had no pediatric intensive care unit (PICU), he was transferred on the third day of the incident to our PICU for further management.

Clinical examination revealed the following: blood pressure 120/75 mmHg, heart rate 100/min, respiratory rate 15/min, temperature 37.5°C, Glasgow coma scale 15/15; pain score 5/10. Systemic examination was normal except for swollen, tender, tense and shiny left foot, leg and thigh, presence of flange marks with continuous oozing at medial distal part of his left leg, diminished pulses at left dorsal pedis and left posterior tibialis arteries. The left calf circumference was 37 cm versus 27 cm on the right, left thigh circumference 40 cm versus 34 cm on the right.

Lab investigation results were; hemoglobin 7.3; hematocrit 23.1; white blood cells 4600; platelets 18,000; lactate dehydrogenase 255; creatinine kinase 999 and troponin-I 0.02. Electrocardiogram and chest x-ray were normal. Urine test for hemoglobin was negative. Liver function tests, kidney function tests and serum electrolytes were all within normal limits. Coagulation profile showed PT of more than 120s (immeasurable) mixed 12, PTT of more than 180s (immeasurable), an INR of more than 10 (immeasurable), a fibrinogen degradation products level of more than 6.4 (immeasurable), and fibrinogen less than 0.5g/l (undetected).

Vascular surgery team was consulted for the compartment syndrome; they decided to treat conservatively because of the severe coagulopathy. Fasciotomy most likely would be associated with massive bleeding.

The following treatment was given: 50 ml (5 ampoules) of PSA for toxin neutralization IV, tetanus toxoid 0.5 ml for tetanus prevention IM, packed blood cells 355 ml, fresh frozen plasma 570 ml, cryoprecipitate 10 units, vitamin K 5 mg and platelets 7 units for treatment of DIC and anemia correction, fentanyl infusion and acetaminophen for pain control, inj. meropenem and inj. vancomycin for potential sepsis, epinephrine 0.3 mg IV and hydrocortisone 100 mg IV for drug reaction developed after PSA administration.

Dramatic improvement of the patient's clinical condition was noted with marked regression of the compartment syndrome. The circumference of the left thigh and leg normalized as compared to the unaffected side within 12 hours of treatment. The patient's coagulation profile came back to normal values. Of note, lab errors were excluded by double checking, which was done on two separate blood samples and by comparing them with the results done at the initial hospital in the same day; all results were identical. The patient was discharged home after one week in a good general condition with no residual functional loss or disability.

DISCUSSION

Snakebites are very common in the third world countries. World health organization (WHO), in a recent adopted study, estimated that at least 421,000 envenomations and 20,000 deaths occurred worldwide from snakebite every year, but warned that these figures might be as high as 1,841,000 envenomations and 94,000 deaths. Antivenom therapy is the key to the medical management of snakebite[2].

The literature and the manufacturers of the snake antivenom recommend its early administration; within 6 hours in case of appearance of any local or systemic signs after snakebite, repeated every 4 to 6 hours until definitive improvement of the signs[3,4]. If compartment syndrome develops later (usually 52 hours after envenomations), antivenom therapy is an alternative to fasciotomy[5].

An evidence-based study confirmed the empirical concept that a delayed time to treat should in no way exclude the use of antivenin immunotherapy in the case of African Vieira bites[6]. Delayed administration of antivenin after 3 days, as in our case, proved to be beneficial in treating delayed development of compartment syndrome and DIC. The reasons of treatment failure are usually insufficient, wrong or inactive antivenom and/or a delay in administration[7]. Antivenom therapy could be associated with an immediate hypersensitivity reaction type I, which should be treated promptly without discontinuation of the antivenom as well as serum sickness type-III[8].

Case reports demonstrate that delayed administration of antivenom may be beneficial for patients with coagulopathies and local symptoms greater than six hours after envenomation[7]. Optimal dosing beyond an 18 hour period has not been established to date and there are no prospective data evaluating the efficacy of polyvalent immune Fab (FabAV) in patients presenting with severe envenomation. Additionally, no prospective studies have been conducted comparing FabAV to other treatments for snakebite envenomations, such as antivenin (Crotalidae) polyvalent (ACP) or observation alone. 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[4,9]. A case series by Lavonas et al. reported 28 patients with severe envenomation, all with clinical improvement after optimal dosing beyond an 18-hour period[8].

CONCLUSION

Antivenin should ideally be administered as early as possible. However, in third world countries, time to treat generally exceeds 24 hours. The positive results of the present case report confirm an empirical concept: a delayed time to treatment should in no way contraindicate the use of antivenin immunotherapy. Antivenin administration should be considered in patients with envenomations complicated by marked and progressive local signs, delayed systemic signs and laboratory abnormalities more than 24h after envenomation despite administration of earlier dose.

REFERENCES

1. Gold, Barry S.; Richard C. Dart, Robert A. Barish. "Bites of venomous snakes". The New England Journal of Medicine.

   2002;347(5):34756.

2. World Health Organization (2007) Rabies and envenomings. A neglected public health issue: Report of a consultative meeting. Geneva: WHO; Available:

   Http://www.who.int/bloodproducts/animal_sera/Rabies.pdf.

3. Rosen PB, Leiva JI, Ross CP. Delayed antivenom treatment for a patient after envenomation by Crotalus atrox. Ann Emerg Med 2000;35:86-88.

4. Bebarta V, Dart RC. Effectiveness of delayed use of crotalidae polyvalent immune Fab (ovine) antivenom. J Toxicol Clin Toxicol. 2004;42(3):321-4.

5. Gold BS, Barish RA, Dart RC, Silverman RP, Bochicchio GV. Resolution of compartment syndrome after rattlesnake envenomation utilizing non-invasive measures. J Emerg Med 2003;24(3):285.

6. Larréché S, Mion G, Mayet A, Verret C, Puidupin M, Benois A, et al. Antivenin remains effective against African Viperidae bites despite a delayed treatment. Am J Emerg Med 2011;29(2):155-61.

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. Lavonas EJ, Kokko J, et al. Short-Term Outcomes After Fab Antivenom Therapy for Severe Crotaline Snakebite. Ann Emerg Med 2011;57(2):128-137

9. Rosen PB, Leiva JI, Ross CP. Delayed antivenom treatment for a patient after envenomation by Crotalus atrox. Ann Emerg Med 2000;35:86-88.

Peer Review

"There seems to be no study too fragmented, no hypothesis too trivial, no literature too biased or too egotistical, no design too warped, no methodology too bungled, no presentation of results too inaccurate, too obscure, and too contradictory, no analysis too self-serving, no argument too circular, no conclusions too trifling or too unjustified, and no grammar and syntax too offensive for a paper to end up in print."

Drummond Rennie

Deputy Editor,

Journal of the American Medical Association

"The mistake, of course, is to have thought that peer review was any more than a crude means of discovering the acceptabilitynot the validityof a new finding. Editors and scientists alike insist on the pivotal importance of peer review. We portray peer review to the public as a quasi-sacred process that helps to make science our most objective truth teller. But we know that the system of peer review is biased, unjust, unaccountable, incomplete, easily fixed, often insulting, usually ignorant, occasionally foolish, and frequently wrong."

Richard Horton

Editor, *The Lancet.*