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Rhabdomyolysis and renal failure of snake bite in pediatric: A case report

Rismala Dewi; Niken Wahyu Puspaningtyas; Steven Mattarungan*

***Corresponding Author: Steven Mattarungan**

Department of Child Health, Universitas Indonesia Medical School/Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Email: stevenmattarungan@yahoo.co.id

Abstract

Venomous snake bites are a global health hazard and is a noteworthy cause of mortality and morbidity especially in Southeast Asia. Improper and delayed treatment of patients with snake envenomation could lead to severe complications and even death. The case was a seventeen-year-old boy presenting with a cobra snake bite on the right lower arm 23 hours prior to admission to the emergency unit. Muscle cramps, pain, and three classic symptoms of rhabdomyolysis: myalgia, weakness, and dark coloured urine were found. On the course of the treatment, this patient was given a repeated dose of SABU (5 times), antibiotics, tetanus immunoglobulins and tetanus toxoids, and other supportive treatments. The patient was discharged due to alleviation of symptoms, with a necrotic wound, which can be seen as a dubious prognosis, due to the possibility of the formation of contractures, and stiffening.

Keywords

snake envenomation; snake bite; rhabdomyolysis; renal failure; paediatrics.

Abbreviations

SABU: Serum Anti Bisa Ular.

Introduction

Venomous snake bites are a global health hazard, as it is a noteworthy cause of mortality and morbidity, especially in South and Southeast Asia, Sub-Saharan Africa, and Latin America [1]. Snake bites is regarded as one the most neglected diseases in the tropics, due to its lack of attention from the government, insufficient incidence reporting mechanisms, which resulted in an increase death rate over the years [2]. Snake bites happen to at least 1.8–2.7 million people in the world every year, resulting in 81,410 to 137,880 deaths. Most of these numbers came from South East Asia, with 1.2–2 million snake bite cases and

57,000–100,000 deaths per year [2,3]. In Indonesia, there were approximately 12,739–214,883 snakebite cases and an estimated of 20–11,581 deaths due to snake envenomation in 2007. However these estimated numbers might not be completely accurate since incidences are more frequent in rural areas and are traditionally treated thus not detected in epidemiological data [4].

Snake bites venom is composed of enzymes and low weight peptides that have several pathological properties [5]. Toxins in snake venoms cause damage to the nervous system, muscles, the blood, and the kidneys [6]. Some venoms have neurotoxic properties that target the presynaptic and/or postsynaptic Neuromuscular Junction (NMJ). The venom contains neurotoxic polypeptides and PLA2 [7,8]. On the presynaptic part, the toxins damage the terminal nerve fibres [8]. On the postsynaptic part, the toxins competitively bind to acetylcholine receptors on the motor endplate, inhibiting action potential thus inhibiting muscle contraction [8]. This effect is especially fatal if affecting muscles of the cardiorespiratory system. Patients rarely experienced impaired consciousness since neurotoxins could not pass through the blood brain barrier [8,9]. Snake venom also contains metalloproteinase, a protease enzyme, that is myotoxic [7]. This enzyme, along with PLA2 damages the tissue of skeletal muscles, that can further cause rhabdomyolysis [10]. Rhabdomyolysis is a condition caused by injury of skeletal muscles, involving leakage of intracellular contents (creatinine kinase, myoglobin, and potassium and phosphor ions [10,11]. Patients with rhabdomyolysis exhibit a triad of symptoms: Weakness, myalgia, and myoglobinuria, described as tea-coloured urine. PLA2 could also cause damage to the myocardium by inducing necrosis to cardiomyocytes [10,12]. Snake venom, specifically venom of the *Viperidae* family, contains a procoagulant enzyme, serine protease [7]. This enzyme promotes the clotting cascade by activating prothrombin [9]. This process activates the blood clotting mechanism which results in blood clots [13]. Added to that, the zinc metalloproteinase found in snake venoms could also directly damage human blood vessels [14]. Because of these mechanisms, persistent bleeding from entry wounds, spontaneous bleeding from gums, subconjunctiva, retroperitoneal, and intracranial space as a sign of disturbances in the blood clotting cascade can be found in patients with snake bites [15]. The hypercoagulative nature of snake venom could also cause deep vein thrombosis, lung emboli, and cerebral infarct [15]. Acute Kidney Injury could also be found in patients with snake envenomation. This can be a direct result of injury of blood vessel and parenchymal tissue of the kidney caused by PLA2 dan zinc metalloproteinases in found in vipers, or secondary to hypotension, profuse bleeding, or rhabdomyolysis [7].

Initial treatment in snake bite patients should be cleaning the wound with running water, fixating the area around the bite to minimalize contractions of muscles around the bite, reducing lymphatic drainage, thus preventing further spread of venom [16]. Attempting to suck out the venom from the wound is not recommended since it only reduces 2% of total venom distributed throughout the body and can exert negative pressure on the wound thus promoting further spread of venom and damage to the area around the wound [17,18]. Antivenom in the form G or Y immunoglobulin as a fragment antigen binding taken from horse, mule, or sheep plasma immunized by snake venom is recommended. SABU is the only form of polyvalent snake antivenom produced by PT. Biofarma in Indonesia. The recommend dose is 2 vials (10 ml) for both children and adults [7]. The most ideal administration of SABU should be as soon as possible, however, SABU is still proven to be efficacious in reducing several pathological effects of snake

venom until 24 hours after snake bite. The recommended way of administering SABU is intravenously, diluted in 5ml/kg of isotonic fluid, monitored with an IV pump, with maximum speed of 2ml/minute, administered in 30–60 minutes [7,16]. The intramuscular route results in lower bioavailability of SABU but can be an option if venous access is difficult to obtain. In paediatric patients, in emergency situations, SABU can also be given through intraosseous route [16]. The success of SABU therapy can be seen from the cessation of spontaneous systemic bleeding (within 15–30 minutes), restoration of blood coagulability (within 3–9 hours), normalization of blood pressure in shock (within 30–60 minutes), improvement of motor and sensory abilities (within 30 minutes) with complete reversal within hours (for post-synaptic type snake venom), cessation of active haemolysis and rhabdomyolysis (within hours) [7,16]. SABU can be readministered after 6 hours from the first administration if laboratory tests showed blood clotting disorders have not improved, or after 1 hour if spontaneous systemic bleeding, neurological disorders, or signs of cardiovascular symptoms persist or worsen. Snake bites are considered as an entry would for tetanus, therefor, prophylaxis should be given according to the patient's previous vaccine history [7]. Snakebites could also promote entry of skin flora bacteria, thus the use of antibiotics targeting gram negative bacteria is recommended if there is signs of infection on the wound [19]. Fluid therapy should also be considered if the patient has rhabdomyolysis to prevent acute renal injury [12].

Case Presentation

The patient was a seventeen-year-old boy presenting with a cobra snake bite on the right lower arm 23 hours prior to admission to the emergency unit. The patient was bitten after attempting to feed a cobra snake at a snake compound facility. The snake fangs punctured the patient for around 2 seconds, which afterwards resulted in an active bleeding wound. The patient tried to clean the wound with running water. Ten minutes after, the patient experienced cramps on his right arm, with difficulties contracting his right lower arm. In the next 30 minutes, the patient experience nausea and vomiting, and developed haematuria. Within 8 hours, the patient had progressive swelling of the right lower arm. The patient was then able to access *Serum Anti Bisa Ular* (SABU) 20 hours after the initial snake bite and was given 1 vial of SABU. The swelling progressed up to the right upper arm, with generalized musculoskeletal pain. The patient had a similar history of snake bites 5 years before, where he was bitten by a king cobra snake on his left ankle, and was given 4 vials of SABU, and hospitalized for 3 days.

On examination on arrival in the emergency unit, the patient was conscious and oriented. The patient was hemodynamically stable. The patient also had a fever of 38°C. On his right lower arm, there were entry wounds of a snake bite, with an appearance of bullae, hematoma, and swelling. Motor examination shows reduced muscle tone for upper and lower limbs (upper extremities 3333/555, lower extremities 5555/5555), declining 17 hours later (upper extremities 3333/4444, lower extremities 4444/4444). Upon observation of diuresis for 17 hours, the patient was oliguric with urine output of 0.43/kg/hour. Other systemic examination was unremarkable. The patient was given 2 vials of SABU 23 hours after the initial snake bite.

The laboratory investigations were as follows: Haemoglobin 15.3 g/dL, haematocrit 43%, thrombocytes 302,000/µL, leucocytes 10,070/µL, with differential count of 0.2% basophil, 0.1% eosinophiles, 77% neutrophiles, 13.2% lymphocytes, and 88% monocytes, random blood glucose 122 mg/

dL, sodium 133 mEq/L, potassium 4.7 mEq/L, chloride 102.5 mEq/L, SGOT 59 U/L, SGPT 85 U/L, urea 21.2 mg/dL, creatinine 0.7 mg/dL, glomerular filtration rate 94ml/min/1,73m^2, PT 1,1 times more than, APTT 1,1 times more than INR. Arterial blood gas revealed pH 7.47, pCO_2 24.5 mmHg, pO_2 112 mmHg, HCO_3^- 18.3 mmol/L, total CO_2 19.1 mmol/L, base excess -2.8 mmol/L, SpO_2 98%. Urine examination showed pH 5.5, traces of albumin, and erythrocyte 1+. From these results it was concluded that the patient had elevated transaminase enzymes, haematuria, and respiratory alkalosis.

The patient was diagnosed as snake envenomation, AKI, rhabdomyolysis, and paraparesis due to snake bite. The patient was treated with 2 vials of SABU diluted in 100 ml of 0.9% NaCl administered within 1 hour (2 hours after the second dose of SABU), ampicillin IV 2 grams every 6 hours, gentamycin 180 mg IV every 8 hours, paracetamol 500 mg PO every 8 hours, ketorolac IV 30 mg every 8 hours if visual analogue scale of pain >5, tetanus immunoglobulin 250 IU, tetanus toxoid 1 ml, and ringer lactate 1,.5 times more than maintenance volume with a target diuresis of 2 ml/kg/hour. Debridement was planned after the patient was stabilized. The patient was then administered to the Paediatric Intensive Care Unit (PICU).

On admission to PICU the patient had declining lower extremities motor function (4444/4444 to 3333/3333). The patient was administered his fourth dose of SABU, 6 hours after the 3rd dose. After one day, the patient experienced less cramps in all four extremities and was able to move them more freely. However, his would appear more necrotic, with sweeling until his right arm and appearance of bullae and hematoma. Urine colour was yellow. The patient had not experienced fever in 24 hours. On examination, muscle strength was 3333/5555 for the upper extremity and 5555/5555 for the lower extremities. The next laboratory investigation was as follows: SGOT 105U/L, SGPT 56 U/L, albumin 2.78 g/dL, Lactate dehydrogenase (LDH) 366 U/L, Creatinine kinase (CK) 4750 U/L, Creatinine kinase muscle brain (CKMB) 81.4 U/L, chloride 102 mEq/L. Twenty-four-hour observation for urine output was 1.3 ml/kg/hour. These results showed elevated transaminase enzymes, hypoalbuminemia, elevated LDH, CK, and CKMB. After the 5th dose of SABU, the patient was transferred out of the PICU to the pediatric ward.

Table 1: SABU administration for the patient.

SABU	Dose of SABU	Rationale of use	Time after onset
1	1 vial (5 ml)	First administration of SABU	20 hours after bite
2	2 vial (10 ml)	First dose was not the recommended dose	3 hours after first dose
3	2 vial (10 ml)	Persistent neurological symptoms	10 hours after second dose
4	2 vial (10 ml)	Worsening of neurological symptoms	6 hours after third dose
5	2 vial (10 ml)		8 hours after fourth dose

After 3 days of care in the paediatric ward, the patient experienced an improvement of initial complaints of extremity weakness and pain. The entry wound appeared necrotic, with the size of 10 X 15 cm. The patient still experienced arm sweeling up to the right shoulder. Laboratory results on day 6 of hospitalization were as follows: Hemoglobin 12.1 d/dL, thrombocytes 216,000/µL, leucocytes 9,170/µL. D-dimer 240 µg/L, fibrinogen 662.4 g/dL, aPTT 1.3 times INR, PT 0.9 times INR. Coagulopathy was not observed based on these results. The patient was then discharged and was scheduled for outpatient clinic visits.

Figure 1: Wound appearance on the patient.

Discussion

The case was about a 17-year-old patient with a venomous snake bite 23 hours before admission to the hospital. The patient admitted to cleaning his wounds with running water for 5 minutes after onset of bite and immobilized his hand with a band aid. In the event of a snake bite, the first aid should be cleaning the wound with running water and soap and immobilizing the area of bite with a firm platform. The patient needs to minimalize movement to slow spread of venom. The patient also needs to immediately seek help to a health care facility, considering delay of SABU administration could be proven fatal in cobra bites [7].

Venoms in cobra snakes have neurotoxin properties. Patients with cobra bites might experience weakness of limbs or cramps just as early as a few minutes after onset [15]. This patient experience muscle cramps and difficulty moving his affected hand after 10 minutes of initial snake bite. The patient does not experience ptosis, ophthalmoplegia, dysphagia, or breathing difficulties. Neurotoxins in snake venom also does not directly cause impaired consciousness since its does not pass through the blood brain barrier. It is also seen in this patient. Immediately after the bite, this patient has signs of local inflammation with mild pain in the entry wound. This symptom is caused by increased vascular permeability caused by inflammatory mediators such as histamine, serotonin, kinins and membrane cell damage caused by proteases. Pain in the entry wound is not specific to snake bites, some snake bites do not cause any pain at all, due to neurotoxins that cause loss of sensation in the area bitten [13,15].

The patient in the case was given 1 vial of SABU 20 hours after onset. This is not ideal since SABU should be given as soon as possible to prevent complications from snake venom. However, SABU still could be given to prevent further disabilities. The initial dose for the patient is less than recommended. According to PT Biofarma, the producer of SABU, the patient should be given 2 vials (10 ml) of SABU for every dose [7].

The patient experience pain in joints, bones, and red coloured urine due to myotoxic properties of snake venom [12]. Myotoxic snake venom, which consists of PLA2 and metalloproteinases cause damage to muscle tissue, specifically skeletal muscle [15]. In the case of rhabdomyolysis, muscle cells release intracellular contents that is toxic to the kidneys [11]. This patient had elevated creatinine and albumin and blood was found in the patient's urine, which indicates damage to the glomerulus. In this patient we

can also see the three classic symptoms of rhabdomyolysis: Myalgia, weakness, and dark colored urine. However, definitive diagnosis can be made if there is an elevated creatinine kinase 5 times the normal value. This patient did not experience consumptive coagulopathy since we did not find reduced number of platelets, fibrinogens, prolonged PT and APTT, or elevated D-dimers [13].

This patient was administered a Ringer Lactate solution 1.5 times maintenance fluids with a target diuresis of 2 ml/kg/hour. This was done to prevent worsening of acute renal failure in rhabdomyolysis.

The target diuresis in rhabdomyolysis should be 4 ml/kg/hour [10]. On urinalysis, it was found that the patients urine had a 5.5 pH. Acidic urine can worsen kidney damage experienced by the patient. Therefore, alkalization in fluid therapy should be added by administering bicarbonate with a target of urine pH of >6.5. Fluid therapy can be stopped if creatinine kinase reached its normal values [7].

The patient was given repeated dose of SABU 10 hours after the initial dose because persistent limb weakness. The patient was given 2 vials of SABU dissolved in 100 ml of 0.9% of NaCl in 1 hour. Repeating the dosage of SABU is appropriate in this patient. SABU can be repeated after 6 hours from the first administration if laboratory tests showed blood clotting disorders have not improved, or after 1 hour if spontaneous systemic bleeding, neurological disorders, or signs of cardiovascular symptoms persist or worsen [7]. This patient did not show blood clotting disorder and signs of spontaneous bleeding. However, this patient showed signs of neurological deterioration, which manifests as reduced motor strength. Therefore, giving this patient another dose of 10 ml of SABU is appropriate.

For antibiotics, this patient was given 2 grams of ampicillin every 6 hours, 180 mg of gentamycin every 8 hours to prevent infection. Empiric antibiotics are only appropriate if the initial entry wound is necrotic or have been manipulated before [19]. From history taking, physical examination, and laboratory workup, it was found that this patient had fevers, pain and necrotic appearance of entry wound in the right arm, and elevated leukocytes, which indicates in infected would, therefor, antibiotic use was proper. The empirical therapy given targets gram negative bacteria normally found on the skin surface.

Administration of tetanus immunoglobulin and tetanus toxoid vaccine is appropriate. Any bite marks should be considered a potential tetanus entry site therefor the two above should be given in accordance to the patient's history of immunization. Since this patient tetanus vaccine history is not clear, this patient was given tetanus toxoid vaccines and tetanus immunoglobulin. The dose given to this patient was correct, 250 IU IM given right after onset of bite [16].

The patient has a dubious prognosis. SABU administration in this patient was delayed, therefore he was given a more aggressive and prolong therapy, and he was at risk of higher mortality and long-term complications [20]. This patient has a necrotic wound, which can result in muscle contractures, joint stiffness, and permanent disabilities. This patient has not experienced brain haemorrhage of ischemia that can result in permanent neurologic deficits.

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References

1. Chippaux JP. Snakebite envenomation turns again into a neglected tropical disease! J Venom Anim Toxins Incl Trop Dis. 2017; 23: 38.

2. World Health Organization. Prevalence of snakebite envenoming. 2021.

3. Gutiérrez JM, Calvete JJ, Habib AG, Harrison RA, Williams DJ, Warrell DA. Snakebite envenoming. Nat Rev Dis Primers. 2017; 3: 17063.

4. Adiwinata R, Nelwan EJ. Snakebite in Indonesia. Acta Med Indones. 2015; 47: 358–65.

5. Fatah C. Pathophysiological and Pharmacological Effects of Snake Venom Components: Molecular Targets. J Clinic Toxicol. 2014.

6. Ranawaka UK, Lalloo DG, de Silva HJ. Neurotoxicity in Snakebite—The Limits of Our Knowledge. White J, editor. PLoS Negl Trop Dis. 2013; 7: e2302.

7. World Health Organization, Regional Office for South-East Asia. Guidelines for the management of snakebites. 2016.

8. Fagerlund MJ, Eriksson LI. Current concepts in neuromuscular transmission. British Journal of Anaesthesia. 2009; 103: 108–14.

9. Shelke RRJ, Sathish S, Gowda TV. Isolation and characterization of a novel postsynaptic/cytotoxic neurotoxin from Daboia russelli russelli venom: Postsynaptic neurotoxin from D. r. russelli. The Journal of Peptide Research. 2002; 59: 257–63.

10. Mannix R, Tan ML, Wright R, Baskin M. Acute Pediatric Rhabdomyolysis: Causes and Rates of Renal Failure. PEDIATRICS. 2006; 118: 2119–25.

11. Petejova N, Martinek A. Acute kidney injury due to rhabdomyolysis and renal replacement therapy: a critical review. Crit Care. 2014; 18: 224.

12. Cheng X, Zhang X. The Analysis of the Treatment of Rhabdomyolysis by Snake Bites. YM. 2018;02:89–94.

13. J White. Snakebites worldwide: Clinical manifestations and diagnosis. Up To Date [Internet]. Available from: https://www.uptodate.com/contents/snakebites-worldwide-clinical-manifestations-and-diagnosis?search=snake%20bite&source=search_result&selectedTitle=2~49&usage_type=default&display_rank=2

14. Chérifi F, Laraba-Djebari F. Isolated biomolecules of pharmacological interest in hemostasis from Cerastes cerastes venom. Journal of Venomous Animals and Toxins including Tropical Diseases. 2013; 19: 11.

15. Teixeira C de FP, Fernandes CM, Zuliani JP, Zamuner SF. Inflammatory effects of snake venom metalloproteinases. Mem Inst Oswaldo Cruz. 2005; 100: 181–4.

16. J White. Snakebites worldwide: Management. Up To Date [Internet]. Available from: https://www.uptodate.com/contents/snakebites-worldwide management?search=snake%20bite&source=search_result&selectedTitle=1~49&usage_type=default&display_rank=1#H10688182

17. Alberts MB, Shalit M, LoGalbo F. Suction for venomous snakebite: a study of "mock venom" extraction in a human model. Ann Emerg Med. 2004; 43: 181–6.

18. Bush SP. Snakebite suction devices don't remove venom: they just suck. Ann Emerg Med. 2004; 43: 187–8.

19. Kularatne S, Kumarasiri P, Puspakumara S, Dissanayaka W, Ariyasena H, Gawarammana I, et al. Routine antibiotic therapy in the management of the local inflammatory swelling in venomous snakebites: results of a placebo-controlled study. Ceylon Med J. 2009; 50: 151.

20. Isbister GK, Brown SGA, Page CB, McCoubrie DL, Greene SL, Buckley NA. Snakebite in Australia: A practical approach to diagnosis and treatment. Medical Journal of Australia. 2013; 199: 763–8.

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Authors Information: Rismala Dewi; Niken Wahyu Puspaningtyas; Steven Mattarungan*
Department of Child Health, Universitas Indonesia Medical School/Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

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