

## Case Report

# Severe coagulopathy and transient hypertension following a *Rhabdophis subminiatus* bite: a case report

Erni Juwita Nelwan<sup>[1]</sup>, Randy Adiwinata<sup>[2]</sup>, Siti Handayani<sup>[3]</sup> and Ikhwan Rinaldi<sup>[4]</sup>

[1]. Division of Tropical and Infectious Disease, Department of Internal Medicine, University of Indonesia, Jakarta, Indonesia. [2]. Faculty of Medicine, Atmajaya Catholic University of Indonesia, Jakarta, Indonesia. [3]. Division of Plastic Surgery, Department of Surgery, University of Indonesia, Jakarta, Indonesia. [4]. Division of Hematology and Medical Oncology, Department of Internal Medicine, University of Indonesia, Jakarta, Indonesia.

### Abstract

Because the majority of colubrid species are considered harmless to human beings, colubrid snakebites are rarely reported. However, the venom of *Rhabdophis*, which is part of the Colubridae family, is procoagulant and leads to severe coagulopathy. Here, we present a case of disseminated intravascular coagulation with enhanced fibrinolysis following a *Rhabdophis* bite. Although coagulopathy can be treated effectively with the specific *Rhabdophis* antivenom, this antivenom is not widely available in Indonesia. We also found transient hypertension secondary to the colubrid venom, an unusual finding.

**Keywords:** *Rhabdophis*. Disseminated intravascular coagulation. Fibrinolysis. Transient hypertension.

### INTRODUCTION

Colubridae envenomation cases are rarely reported and as such are greatly understudied<sup>(1)</sup>. The clinical manifestations of envenomation vary from mild to severe systemic conditions, such as bleeding, renal failure, and shock<sup>(2)</sup>. In addition, the primary treatment for bites by *Rhabdophis* species is administration of the specific antivenom<sup>(3)</sup>; however we herein report the case of a patient with severe coagulopathy and unusual transient hypertension secondary to *Rhabdophis* envenomation who recovered with polyvalent equine antivenom.

### CASE REPORT

A 59-year-old man presented to the emergency room with urogenital bleeding that had lasted for 3 days accompanied with gingival bleeding and hematomas in his lateral right thigh and dorsal left hand. He was bitten on his dorsal right hand by a snake 5 days before admission. There was no history of nausea, vomiting, drowsiness, convulsions, pain, or fever, and there was no significant past history related to blood coagulation disorders. As shown in **Figure 1** the anamnesis revealed that the snake was a red-necked keelback snake (*Rhabdophis subminiatus*).

Upon physical examination, the patient looked moderately ill and had a blood pressure of 130/80mmHg. Results of his general examination were normal; however, the local examination

showed signs of a subcutaneous hematoma around the bite mark site on dorsal right hand (**Figure 2**).

Initial hematological and biochemical investigations, including a complete blood count, liver and renal function tests, an electrolyte panel, and random blood glucose level examinations were normal. Electrocardiography and chest X-ray were also normal. Hemostatic parameters revealed an activated partial thromboplastin time (aPTT) >180 seconds (control: 27.9-37.0 seconds), a prothrombin time (PT) >120 seconds (control: 12.3-15.3 seconds), immeasurable D-dimer, and a fibrinogen level of 5mg/dL. Based on these results, the patient was diagnosed with disseminated intravascular coagulation (DIC) with enhanced fibrinolysis secondary to snakebite envenomation. To restore coagulation factor levels, he was treated with tranexamic acid (1 gram/8 hours), vitamin K, fresh frozen plasma (FFP), and cryoprecipitate. However, only transient improvements to the hemostatic parameters were seen, and, during 12 hours monitoring, his fibrinogen level progressively declined even though the patient continued to receive cryoprecipitate transfusions and FFP.

Antivenom was not administered initially because based on the clinical practice it should be given within 72 hours after bitten by the snake while the patient visited the hospital later than that. Unfortunately supportive treatment showed unfavorable results, therefore antivenom was eventually administered on day 7 of hospitalization. Two vials (10mL) of polyvalent antivenom (Biosave®) were diluted in 500mL of normal saline solution and administered for 3 hours following diphenhydramine (as premedication). The patient reported a fever (38°C) during antivenom administration but there were no other adverse

**Corresponding author:** Erni Juwita Nelwan, MD  
**e-mail:** ejnelwan@yahoo.com  
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FIGURE 1. *Rhabdophis subminiatus* and bite mark.



FIGURE 2. Subcutaneous hematoma around the bite mark.

effects. His fibrinogen level increased to 62mg/dL the following day. The antivenom serum was readministered on days 8 and 9 following the same protocol. The patient's hemostatic parameters improved each day without the use of hemostatic drugs or blood products. On day 13, the patient's symptoms had disappeared and he was discharged with a PT of 15 seconds (control: 12 seconds), an international normalized ratio (INR) of 1.35 (control: 0.89), an aPTT of 35 seconds (control: 36 seconds), a fibrinogen level of 100mg/dL, and a D-dimer level of 631mcg/L.

During hospitalization, the patient also developed grade II hypertension with a blood pressure of 150/100mmHg even though he had no prior history of hypertension. His renal function tests were normal, and we successfully managed the hypertension with amlodipine uptitrated to 10mg once daily.

During outpatient monitoring, the patient's hemostatic parameters returned to normal within 2 weeks and no further antihypertension drugs were needed.

## DISCUSSION

There are two most known species of Colubridae: *Rhabdophis tigrinus* and *Rhabdophis subminiatus*. Several cases of *Rhabdophis tigrinus* bites have been reported in Japan but very few cases of *Rhabdophis subminiatus* bites have been reported<sup>(3) (4)</sup>. The bites of colubrid snakes can lead to severe envenoming, but the symptoms of such bites might be delayed for hours or days after the actual bite<sup>(2)</sup>.

The hematuria and hematomas in our patient were caused by DIC with enhanced fibrinolysis. DIC was identified by a prolonged PT and aPTT value as well as a high D-dimer level; however, transfusion with FFP and cryoprecipitate provided only transient hemostatic improvement. This is most likely because Colubridae venom contains serine protease and other procoagulant enzymes that can stimulate fibrin formation in the blood stream. After a bite, plasmin immediately degrades the fibrin clot resulting in coagulation factor depletion<sup>(3)</sup>. DIC will persist as long as venom is still circulating in the blood.

Disseminated intravascular coagulation with enhanced fibrinolysis is typically described as small increased of plasminogen activator inhibitor and fibrinolysis related to activation of coagulation. Therefore, the formed multiple microthrombi caused by hemostasis are rapidly dissolved. As a result, end organ damage rarely occurs but severe bleeding manifestations are common. The diagnostic criteria for DIC with enhanced fibrinolysis includes an elevated thrombin-antithrombin complex ( $\geq 20\mu\text{g/L}$ ), a plasmin- $\alpha_2$  complex  $\geq 10\mu\text{g/L}$ , a fibrin degradation product (FDP) level  $\geq 80\mu\text{g/L}$ , a fibrinogen level  $< 100\text{mg/dL}$ , and an increased FDP/D-dimer ratio<sup>(5)</sup>. Other useful hemostatic tests include a 20-minute whole blood clotting test, a PT test, an aPTT test, and an INR test<sup>(6)</sup>. The main treatment for coagulopathy due to venom is antivenom administration; however, allergic reactions, high cost, and unavailability often limit its use<sup>(2)</sup>. For example, although Hifumi et al. have demonstrated the effectivity of *Rhabdophis* specific antivenom<sup>(7)</sup>, in Indonesia, the only available snake antivenom is a polyvalent equine antivenom indicated for the treatment of *Naja sputatrix*, *Bungarus fasciatus*, and *Agkistrodon rhodostoma* envenomation<sup>(8)</sup>. However, after administering six vials of this antivenom, we saw improvements in the patient's hemostatic parameters suggesting a potential for cross-neutralization<sup>(9)</sup>. However, more studies are needed to confirm these results, and whenever available specific antivenom must be used first and should be made widely available in countries with a high risk of snake envenoming, such as Indonesia.

Antivenom should be administered as soon as possible; however, antivenom administration is often delayed more than 24 hours. In the present case, the administration of antivenom was still effective even though the administration was delayed 9 days after the first symptoms developed. This supports results from a similar report by Al-Hashaykeh et al. and indicates that antivenom can be administered while coagulopathy persists<sup>(10)</sup>.

Finally, even though our patient had no previous history of hypertension, we found high blood pressure during hospitalization and treated the patient with an antihypertensive drug. The role of Colubridae snake venom in causing hypertension

is unclear. However, Viperidae and Elipidae venom has cardiotoxic effects that can induce autonomic dysregulation and catecholamine release<sup>(11)(12)</sup> potentially leading to hypertension; therefore, snakebite patients should be monitored for transient hypertension secondary to snakebite venom.

In conclusion, snakebite was a potential harmful condition with a limitation of specific antivenom availability. The decision to administer antivenom needs to be tailored for each case. Indeed, early administration will lead to better outcomes.

#### Conflicts of Interest

The authors declare that there is no conflict of interest.

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