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CASE REPORT

Neurological Involvement and Hepatocellular Injury Caused by a Snake With Hematotoxin Envenomation

Watchareewan Sontichai, MD; Sanit Reungrongrat, MD; Paitoon Narongchai, MD; Rungrote Natesirinilkul, MD

From the Department of Pediatrics (Drs Sontichai, Reungrongrat, and Natesirinilkul); and the Department of Forensic Medicine (Dr Narongchai), Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.

Venomous snakes with hematotoxin—Russell's viper (*Daboia* spp), Malayan pit viper (*Calloselasma rhodostoma*), and green pit viper (*Cryptelytrops albolabris and C macrops*, previously named *Trimeresurus* spp) are commonly found in Thailand. Coagulation factor activation, thrombocytopenia, hyperfibrinolysis, and disseminated intravascular coagulation are the main mechanisms of hemorrhaging from these snake bites. The neurological involvement and hepatocellular injury after Russell's viper bites were reported in Sri Lanka, but there is no report from Southeast Asia. This case was a 12-year-old hill tribe boy who had ptosis and exotropia of the left eye, respiratory distress, and prolonged venous clotting time, prothrombin time, and activated partial thromboplastin time; low fibrinogen and platelet count; and transaminitis after being bitten by a darkish-colored snake. He did not respond to antivenom for cobra, Malayan pit viper, or Russell's viper. However, his neurological abnormalities, respiratory failure, and hepatocellular injury improved, and coagulopathy was finally corrected after receiving antivenom for green pit viper. The unidentified snake with hematotoxin was alleged for all manifestations in this patient.

Key words: neurological abnormality, ptosis, exotropia, hepatocellular injury, coagulopathy, snake bite

Introduction

Russell's viper (*Daboia* spp), Malayan pit viper (*Calloselasma rhodostoma*), and green pit viper (*Cryptelytrops albolabris and C macrops*; previously named *Trimeresurus* spp) are known as venomous snakes with hematotoxicity.[1] All of them are classified in the family Viperidae and are called vipers. They are commonly found in every region of Thailand.[1–9] Although their toxin, hematotoxin, cause bleeding disorders, the mechanisms of each hematotoxin are different. Russell's viper toxin activates factor V and X and, moreover, can cause disseminated intravascular coagulation (DIC), whereas the Malayan and green pit viper toxins have thrombin-like effects that cause hypofibrinogenemia, thrombocytopenia, and hyperfibrinolysis.[5–8] Bleeding disorders, local swelling, and pain of the affected areas are the common presentations of patients bitten by snakes with hematotoxin.[1,5–9] The toxicity of a Russell's viper bite has been reported to cause neurological symptoms[10–12] and liver injury.[13] Neurological involvement without intracranial bleeding and liver injury as a result of the bite of a snake with hematotoxin has never been reported in Thailand.

We report the case of a boy who had ptosis, exotropia, respiratory failure, rhabdomyolysis, and transaminitis after being bitten by a darkish-colored snake, which was not captured. He did not respond to antivenom for cobra, Malayan pit viper, or Russell's viper. His neurological and respiratory abnormalities, coagulopathy, and hepatocellular injury finally recovered after receiving antivenom for green pit viper.

Case Presentation

A 12-year-old hill tribe boy, previously healthy, presented with swelling and pain in his left leg after being bitten on his left ankle by a snake in the forest while he was playing with a friend 2 days before he came to Maharaj Nakorn Chiang Mai University Hospital (MNCMUH). The patient described the snake as a 1-foot-long, darkish-colored snake. After the snake bite, the patient had gradual and continuous oozing from the bite wound without bleeding from other sites. One day

Corresponding author: Rungrote Natesirinilkul, MD, Department of Pediatrics, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand (e-mail: rungrote.n@cmu.ac.th).

later, he had more swelling and pain in his left leg. He was taken to the local hospital 26 hours after the snake bite. His vital signs were assessed as follows: temperature 36.2ºC, pulse rate 94 beats/min, respiratory rate 20 breaths/min, and blood pressure 140/90 mm Hg. His oxygen saturation was 90% at room air, which was corrected by oxygen supplementation. The physical examination showed blood oozing from the wound and swelling of the left leg. Mild ptosis of the left eye was also noted. Neurological examination was otherwise normal. The initial evaluation of blood tests revealed hemoglobin of 15 g/dL, white blood cell count of 16.05 $\times$ 10^3/mm^3, platelet count of 224 $\times$ 10^3/mm^3, creatinine 0.57 mg/dL, prothrombin time (PT) greater than 180 seconds, activated partial thromboplastin time (APTT) more than 180 seconds, and venous clotting time (VCT) more than 30 minutes. Because of the desaturation and prolonged coagulation tests, he was treated with 3 doses of antivenom for cobra and Malayan pit viper (Queen Saovabha Memorial Institute, Thai Red Cross Society, Bangkok, Thailand) and 1 dose of tetanus toxoid 0.5 mL and tetanus antitoxin 30,000 units. Despite the treatment, desaturation and prolonged coagulation time were not corrected. After receiving antivenoms, vitamin K, and 6 units fresh frozen plasma, he still had bleeding symptoms and prolonged VCT.

At 51 hours after the snake bite, his left leg became more swollen and inflamed. Ptosis, diplopia, respiratory distress, and red urine developed. He was intubated and then transferred to MNCMUH. Ceftriaxone and amoxicillin/clavulanic acid were given. The physical examination at MNCMUH showed 2 fang marks 0.1 cm in diameter, each with a fang mark distance of 0.8 cm on the left lateral malleolus (Figure 1). He had mild

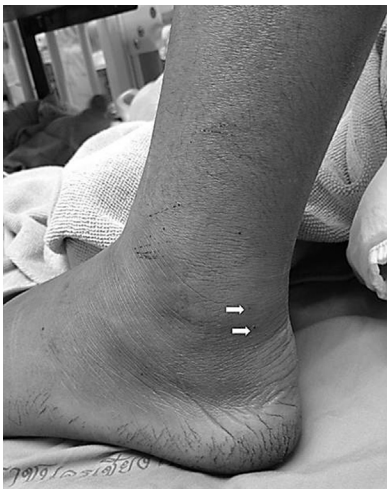

Figure 1. Fang mark on left ankle, below to left lateral malleolus (arrows).

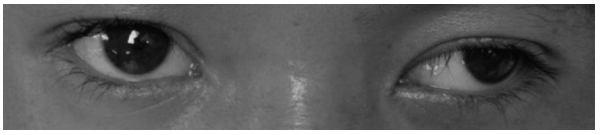

Figure 2. Exotropia and ptosis of the left eye on day 1 of admission.

tenderness and swelling of the left ankle without hemorrhagic bleb or ecchymosis. There was no more oozing from the bite wound and no other bleeding from other sites. He had normal consciousness but ptosis of the left eye with palpable fissure distance 0.9 cm of the left eye while his right eye had the palpebral fissure distance of 1.5 cm. He also had exotropia of the left eye (Figure 2). In addition to ophthalmoplegia, he had paradoxical breathing when he was accidentally extubated despite having normal breath sound on both sides on examination. The blood tests on day 2 after the snake bite were as follows: complete blood count with hemoglobin 10.8 g/dL, white blood cell count 10.2 $\times$ 10^3/mm^3, and platelets 153 $\times$ 10^3/mm^3; blood chemistry with creatinine 0.6 mg/dL, total creatine kinase 135,846 U/L, total protein 6.7 g/dL, albumin 3.4 g/L, alkaline phosphatase 209 U/L, aspartate aminotransferase 3,897 U/L, alanine aminotransferase 1,268 U/L, total bilirubin 0.57 mg/dL, and direct bilirubin 0.07 mg/dL; arterial blood gas showed pH 7.47, pO_2 157 mm Hg and pCO_2 39.8 mm Hg with FiO_2 of 0.4 on ventilator setting; urine analysis showed heme 3+, red blood cell count 2 to 3/high-power field, white blood cell count 20 to 30/high-power field; coagulation tests found PT greater than 200 seconds, APTT more than 200 seconds, VCT greater than 30 minutes, D-dimer 8.5 mg/L, factor X clotting assay 71%, and factor V clotting assay 105%; his chest radiograph was unremarkable. The boy was diagnosed with snake bite and coagulopathy, respiratory failure, and myoglobinuria. He was treated with 5 doses of antivenom for Russell's viper and 1 dose of fresh frozen plasma in 48 hours without any improvement of the clinical symptoms and coagulopathy. Moreover, his platelet count was gradually decreasing to the lowest number, at 125 $\times$ 10^3/mm^3 on day 5 after the snake bite. His blood chemistry gradually improved, however.

After consultation with the institutional toxicologist and Ramathibodi Poison Center at Mahidol University in Bangkok, the patient was treated with antivenom for green pit viper on day 5 after the snake bite. He subsequently had clinical improvement of left ptosis, exotropia, and respiratory weakness within 12 hours after the first dose of antivenom. The coagulation tests also became normal within 6 hours and the platelet count within 24 hours after antivenom treatment. On day 10 of