CASE REPORT

Retrospective Documentation of a Confirmed White-Lipped Green Pit Viper (*Trimeresurus albolabris* Gray, 1842) Bite in the South-Central Hills of Nepal

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This case report documents envenomation by an arboreal white-lipped green pit viper (*Trimeresurus albolabris*), a species found in South and Southeast Asia that causes the majority of venomous snakebites among Southeast Asian pit vipers. Clinical features vary from asymptomatic to serious coagulopathy that may progress into life-threatening or fatal hemorrhage. The proven life-threatening cases described in published literature, however, are sparse. Practically, no specific antivenom targeted to pit viper bites is available in Nepal. We report a case (managed with several non-evidence-based interventions) of noticeable coagulopathic envenomation due to confirmed *T albolabris* bite in Nepal. This is the first known reported case of such a bite in Nepal. This case highlights the urgent need to improve diagnosis, monitoring, and supportive care for bite victims and to study the effectiveness of Thai pit viper antivenoms for the treatment of *T albolabris* envenomations.

Keywords: snakebite, envenomation, hemotoxicity, antivenom, coagulopathy, venom-induced consumption coagulopathy

Introduction

Clinical coagulopathy due to pit viper (*Trimeresurus* species) bites is a common systemic envenomation in Asia.^{1–7} The genus *Trimeresurus* comprises approximately 46 pit viper species.⁸ Little is known about the pit viper species diversity and the burden and effects of bite envenomations. Among the 6 pit viper species with definitive distribution records in Nepal (ie, *Gloydius himalayanus*, *Ovophis monticola*, *Trimeresurus albolabris*, *septrionalis*, *stejnegeri*, and *tibetanus*), *albolabris* (synonym *Cryptelytrops albolabris*) is a common, medically relevant snake that is distributed in the lowlands, hills, and lower ranges in mountains of Nepal.^{9–19} *T albolabris* is also distributed in South and Southeast Asian countries,^{20,21} where they can cause local and systemic

envenomation^{2,22–25} producing painful local swelling, blister formation, necrosis, and coagulopathy.^{2,26–28} Fatalities have probably occurred either primarily or secondarily after *T albolabris* envenomation in Hong Kong²⁴ and Java.²⁶ In Nepal, at least 3 to 8% of snakebites are attributed to *T albolabris*.^{14,17,19,29,30} Despite this, there are no published details on systemic envenomation by pit vipers. Herein, we present clinical manifestations and management practices for a proven *T albolabris* envenomation that occurred in the south-central hills of Nepal. This is the first known reported case of such a bite in Nepal. This case was treated with several non-evidence-based interventions without use of antivenom, potentially making it of additional interest.

Case report

A 17-y-old, relatively healthy boy from Bharatpur Metropolitan City in Nepal was bitten by a *T albolabris* (Figure 1) at 1845 while rescuing the snake, which was resting in a bamboo bush in Gorkha District in the south-central hills of Nepal. The snake that inflicted the

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Submitted for publication May 2018.

Accepted for publication November 2018.

Figure 1. White-lipped green pit viper (*Trimeresurus albolabris*) involved in bite while rescuing it from premises of an herbal company in Gorkha District, Nepal. Photograph by Deb P. Pandey.

envenomation was formally identified by the senior author (DPP) with the keys included in widely used herpetological guidebooks.^{31,32} The victim was bitten on the lateral aspect of his left wrist (Figure 2) while attempting to pick up the snake with his bare hands. He applied a handkerchief to the bite site as a loose ligature (Figure 2). Then he was carried up the road for 25 min and transferred to a bus, which carried him in Laxmi Hospital in Tanahu District, where he arrived 1.5 h after the bite. While riding the bus, he used his own sacred thread *Janai* as an arm sling on the bus and kept his hand below heart level until he reached the hospital.

On admission to the hospital there were 2 distinct fang marks with local bleeding from the bite site and swelling of the wrist, back of the hand, and fingers. About 4.5 h postbite, the swelling extended up the forearm to the elbow (Figure 3). He was treated with antibiotics and a proteolytic enzyme (Table 1). Because of the extension of swelling, he was referred to the Bharatpur Hospital, Chitwan, about 36 h after snakebite (0645). He was referred for surgical consultation at a higher center immediately after initial evaluation in the emergency department of Bharatpur Hospital (1145).

The patient was admitted in College of Medical Sciences, Chitwan, at 1215 (41.5 h after snakebite). On

Figure 2. White-lipped green pit viper (*Trimeresurus albolabris*) bite on lateral aspect of the left hand. Top, immediately after bite, red piece of cloth is a loose tourniquet. Bottom, after reaching to local hospital. Photograph by Amod Ghimire.

examination, there was extensive swelling of the left upper limb up to the left upper part of the chest. Initial laboratory values are described in Table 1. His prothrombin time (PT) remained prolonged on subsequent testing in the fourth, sixth, and seventh days after snakebite. Platelet counts were not performed until 1 wk postenvenomation. Kidney function tests were not performed.

After admission (41.5 h after snakebite), he received ongoing antibiotic therapy, histamine receptor antagonist (ranitidine, 150 mg orally, twice daily), nonsteroidal anti-inflammatory drug (ibuprofen, 400 mg orally, thrice daily), and vitamins (Table 1). Two units of fresh frozen plasma (FFP) were transfused on the sixth day after snakebite.

The swelling gradually subsided, and the patient was discharged on request on the seventh day after the snakebite. He was advised to take similar medicines (Table 1), have the PT tested every alternate day, and return for follow-up.

He returned to the hospital for a follow-up visit on the ninth day after snakebite. His PT had decreased to 38 s and his medications were discontinued. Antivenom was

Figure 3. Swelling shown extending up the forearm to the elbow of the left hand. Healthcare staff cleaned the bite site and dipped the hand in a concentrated potassium permanganate solution that caused erythema-like features on hand. Photograph by Chandra P. Adhikari.

not given to this patient at either hospital. He reported no sequelae of the bite.

Discussion

We report a case of prolonged coagulopathy due to a confirmed bite by *T albolabris* in Nepal.

The patient did not develop any systemic bleeding manifestations. Bleeding was only from the bite site with the normal bleeding time and normal whole blood clotting test (WBCT) at about 42 h postbite. This was seen despite the risk of systemic bleeding due to thrombin-like compounds in *T albolabris* venom.³³ Two cases of envenomation from this species in Thailand³⁴ and 1 from Hong Kong²² involved severe systemic bleeding. A study in Thailand described 54% of cases (n=13) with incoagulable blood and 17% (n=4) with systemic bleeding among 24 cases envenomed by *T albolabris*.² Others have described *T albolabris* as having the potential to cause consumption coagulopathy.³⁵ The risk of systemic bleeding is even greater without the provision of anti-venom. Despite the risk of systemic bleeding, this patient did not undergo sufficient investigations to assess the

possible evolution of systemic coagulopathy. Although thrombocytopenia is a common hematological effect and a hallmark of hematological disorders due to pit viper envenomation,^{23,36–38} platelets were only measured in a single assay that detected mild thrombocytopenia (Table 1). For the proper diagnosis of pit viper bite, platelets should be measured on arrival and serially monitored including for a week or more postdischarge.

The prolonged PT from 41.5 h postbite to the ninth day postbite (Table 1) indicated moderate to severe local envenomation (with mild systemic involvement) due to mild depletion of the fibrinogen resulting in mild consumption coagulopathy.⁷ The prolonged PT was described as occurring in the majority of green pit viper bite cases³⁶ in 1 report and in a single case of suspected pit viper bite.³⁹ Nevertheless, the reports of defibrination syndrome (ie, hypofibrinogenemia) due to *T albolabris* bite elsewhere^{2,3,22,24,40} supported our diagnosis of mild consumption coagulopathy, indicating the risk for life-threatening hemorrhage.^{2,24} Because the WBCT20 has notably variable sensitivity and specificity,⁴¹ the information on conditions in which the assay was run, including the type of tube used, should be provided to better evaluate the profile of efficiency of WBCT. Whenever possible, it is important to run a control sample in parallel using a blood sample drawn from a healthy volunteer.

In addition to coagulopathy, local effects such as intense pain locally and extension of swelling proximally up to the left upper part of the chest in our case were also reported in other cases in parts of Nepal, Bangladesh, Hong Kong, and Thailand^{2,4,22,26–28,37,39} and in the United States (an exotic neonatal *T albolabris* envenomation).⁴² Venom phospholipases A2 and metalloproteases are probably responsible for the local edema that, without treatment, can progress to local blistering and necrosis.^{2,43} The intense swelling and pain experienced by our patient was not associated with the loose ligature (Figure 2), which was used for about 30 min only. In an attempt to reduce the extensive swelling of the bitten part, a non-evidence-based intervention (ie, administration of proteolytic enzyme and antibiotics of doubtful benefit) was used with this patient. There is no evidence supporting this intervention, and it may do harm; therefore, it is contraindicated.

Although bacterial infection may be primary (snake venom and the snake buccal cavity contain bacterial flora)^{25,44} or secondary (affecting necrotic wounds^{45–47} that sometimes develop after pit viper envenomations), antibiotics are not routinely used prophylactically.^{48,49} However, any signs of evolving infection should prompt broad-spectrum antibiotic treatment. Distinguishing infection from venom-induced local effects can be quite

Table 1. Timing, laboratory findings, and management for *Trimeresurus albolabris* bite case in Nepal

Timing	Laboratory findings	Details of management (medication)
1.5 h after snakebite	None	Healthcare staff cleaned the bite site and advised the patient to dip his hand in a concentrated potassium permanganate solution and remove the ligature and thread-sling. The patient was advised to keep his hand below heart level using a cotton sling.
About 4.5 h after snakebite	None	He was treated with ampicillin 500 mg, IV and cloxacillin 500 mg, IV (ie, megapen IV, 1 g, stat; and twice a day); trypsin-chymotrypsin 10 mg, PO (chymoral forte, PO, thrice a day); dextrose 5% II unit, IV (500 mL in each unit, over 24 h).
41.5 h after snakebite	Initial laboratory investigations included white cell count of $10 \times 10^9/L$ (RR: $4-11 \times 10^9/L$), neutrophils 79% (RR: 40–65), lymphocytes 17% (range: 20–45), otherwise normal differential count, and erythrocyte sedimentation rate was 2 mm in first hour (RR: 1–10 mm). His coagulation studies were a bleeding time (Ivy's method) of 3 min (RR: 2–7 min), whole blood clotting time (Lee-White WBCT method), 6 min 30 s (RR: 3–8 min), and PT of greater than 2 min (control 14 s [RR: 12–16 s]).	He received ongoing antibiotic therapy with ampicillin 250 mg, IV and cloxacillin 250 mg, IV (megapen 500 mg, IV, 4 times daily for 4 d); gentamicin 160 mg, IV, once a day for 4 d in addition to metronidazole 500 mg, IV, 3 times a day for 4 d; ranitidine, PO (Aciloc 150 mg, PO, 2 times a day); Flexon, PO (ibuprofen 400 mg and paracetamol 500 mg), orally, 3 times a day; prednisolone, PO (wysolone 10 mg, PO, 3 times a day for 4 d); and neurobion, PO (vitamin B1, B6, and B12), 1 tab once a day for 2 d). He was also given vitamin K (10 mg, intramuscularly, once a day for 5 d).
Fourth post-snakebite day	PT on 2 different occasions more than 1 min.	None
Fifth post-snakebite day	None.	None
Sixth post-snakebite day	PT more than 2 min.	Two units of fresh frozen plasma were transfused.
Seventh post-snakebite day	PT 56 s; platelet count was $165 \times 10^9/L$ (RR: $150-400 \times 10^9/L$).	The patients was discharged on request with the following advice: 1) amoxycillin 250 mg and flucloxacillin 250 mg, PO (ie, capsule megapen 500 mg PO, 4 times a day for 3 d); 2) metronidazole, PO, 400 mg, 3 times a day for 3 d; 3) ranitidine, PO (Aciloc 150 mg, PO, twice a day for 2 d; 4) flexon, PO (ibuprofen 400 mg and paracetamol 500 mg), PO, 3 times a day for 2 d, then as per required (SOS); 5) neurobion (vitamin B1, B6, and B12), 1 tab, PO, once a day for 1 week; and 6) PT measurement every alternate day. He was asked to follow up with the report.
Ninth post-snakebite day	His PT had decreased to 38 s.	Medications were discontinued.

IV, intravenous; PT, prothrombin time; RR, reference range; PO, by mouth

difficult and requires careful evaluation. Pre-emptive use of antibiotics without clear clinical and laboratory evidence is not warranted, but we recommend using tetanus prophylaxis as soon as any coagulopathy has been corrected.^{25,47}

The use of FFP in treating envenomated patients with consumptive coagulopathy who have not received anti-venom may prolong the coagulopathy and increase the

risk of hemorrhage.³⁵ Although swelling gradually reduced after the administration of 2 units of FFP in our case, PT was noticeably prolonged (Table 1). This has been reported previously in Hong Kong.²² FFP supplies clotting factors such as fibrinogens that can be activated by the circulating venom toxins and those toxins absorbed by the uptake of additional venom possibly sequestered at the bite site.^{50,51} A recently conducted

clinical trial investigating envenomed patients with consumptive coagulopathy⁵² suggested that using FFP and antivenom together restored clotting factors more rapidly and reduced clotting time and the amount of antivenom required. FFP was found not to expedite reversal of coagulopathy in patients envenomed by Russell's viper (*Daboia russelii*) in Sri Lanka.⁵³ Because there is no consistent quality evidence supporting provision of FFP even with antivenom,^{50,53} FFP should not be transfused except for clearly defined clinical indications. Otherwise, it may complicate treatment, resulting in prolonged hospital stay and higher treatment costs.

Overall, *T albolabris* envenomation should be treated with proper antivenom⁵¹ available in Thailand⁵⁴ in addition to appropriate supportive care and wound management. Envenomation by this species should be considered serious because it can result not only in mild local effects but also in severe consumptive coagulopathy, placing the patient at the risk of systemic bleeding and death. There is no pit viper antivenom available in Nepal.⁵⁴ The administration of Thai green pit viper antivenom has been shown to reduce severe limb edema, reverse coagulopathy in patients envenomed by pit viper, and neutralize venoms from different pit viper species distributed in Asia.^{27,39,42,43,55,56} It is important to know the effectiveness of Thai green pit viper antivenom against Nepalese pit viper envenomations in speeding recovery. The Nepal government should plan to use Thai hematompolyvalent antivenom if it cross-neutralizes venoms from Nepalese green pit vipers^{39,57} or develop antivenom that covers all Asian pit vipers distributed in Nepal.

In our case, ranitidine was used to reduce the stress-induced hypersecretion of gastric acid despite no administration of antivenom. There is no evidence to support the administration of vitamin B complex or vitamin K for envenomation, and the latter may introduce risk. There is also no evidence for any benefit of using prednisolone⁵⁸ in the treatment of envenomation, aside from its value in preventing serum sickness after the administration of some antivenoms. This is not applicable in our case because no antivenom was administered. Analgesia (nonsteroidal anti-inflammatory medicine [eg, ibuprofen]) can be given to patients without contraindications, given normal renal and coagulation function.⁴² Because our patient had unknown renal function and coagulopathy was not serially monitored, the use of ibuprofen was inappropriate. Kidney injury is possible after envenomation by many viperid species.^{34,59,60} Renal function should be monitored periodically to ensure appropriate supportive care.

The patient used nonstandard first aid measures due to limited knowledge on prehospital care of snakebites.⁶¹

Although controversial when used for viperid envenomation, we support the use of the local compression pad immobilization method⁶² to confine the venom to the affected extremity and reduce systemic absorption. We recommend keeping the bitten body part elevated in all pit viper envenomations to reduce local swelling and minimize local tissue damage.⁶³ Patients should also be transported quickly to receive proper medical care.

Conclusion

White-lipped green pit viper (*T albolabris*) envenomation may be life-threatening in Nepal because of no availability of pit viper antivenom, poor diagnosis and monitoring of the patient, use of non-evidence-based interventions (eg, use of FFP, proteolytic enzymes, antibiotics), and poor knowledge of prehospital care of snakebite. There is a clear need for an evidence-informed, unified algorithm and research on the effectiveness of Thai green pit viper antivenoms for the treatment of pit viper bites in Nepal. Additional clinical and laboratory studies of confirmed pit viper bite are important for proper evaluation. For the proper diagnosis and management of coagulation disorder due to pit viper envenomation, platelet count, bleeding time, PT, activated partial thromboplastin time, thrombin time, plasminogen, fibrinogen, fibrin degradation product, D-dimer level, soluble fibrin monomer, euglobulin clot lysis time, and renal and liver function should all be measured regularly (with special consideration of the risk of bleeding at the site of blood sampling) until normality is restored. This helps to determine venom-induced consumptive coagulopathy and to provide proper supportive care. Snakebite management guidelines in Nepal could be improved by adopting judicious supportive care and pit viper antivenom therapy.

Acknowledgment: The authors thank the hospitals involved for providing treatment details and laboratory reports. They also thank a German volunteer in Nepal who initially carried the patient in the evacuation to local hospital. Moreover, they are grateful to Chandra Prasad Adhikari for the due care of the snakebite victim. They thank Geoff K. Isbister, Clinical Toxicology Research Group, University of Newcastle, Australia, for his initial review of this article and anonymous reviewers for their critical review comments. Written consent for publication of this case history and photographs was obtained from the patient.

Author Contributions: Conceived the study during which the case was recorded, identified the snake, and collected primary data (DPP); drafted the manuscript (DPP, BRS); reviewed the manuscript (DPP, AG, BRS); read and approved the final manuscript (DPP, AG, BRS).

Financial/Material Support: DPP's research on snakebite in Nepal was supported by the South Asian Clinical Toxicology Research Collaboration and NHMRC CRE APP1110343, Australia.

Disclosures: None.

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