CASE REPORT

A Tropical Kiss by a Malabar Pit Viper

Freston Marc Sirur, MD¹; Vrinda Lath, MBBS¹; Chethana A.S., MBBS¹; Ganesh Mohan, MD²; Shamee Shastri, MD²

¹Department of Emergency Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India;

²Department of Immunohematology and Blood Transfusion, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India

Snakebite in India is often attributed to the “big 4,” for which polyvalent anti-snake venom is effective. Also significant and less known is the burden of other venomous snakes, one of which is *Trimeresurus malabaricus*. We report a bite to the face of a tree climber by *Trimeresurus malabaricus* in the Western Ghats of India, which caused severe local envenomation in the form of facial edema and systemic signs of envenomation, including coagulopathy and hypotension. We discuss the role of thromboelastogram, infrared thermography, and routine diagnostics in this case, which led to the administration of Indian-made polyvalent anti-snake venom. The patient recovered and was discharged without any clinically evident physiological or physical dysfunction.

Keywords: *Trimeresurus malabaricus*, envenomation, thromboelastogram, venom induced consumptive coagulopathy, snakebite, antivenom

Introduction

Snakebite is a neglected tropical disease, with India burdened by the highest number of deaths globally. Snakebite is attributed most commonly to the “big 4,” namely, the Russell’s viper (*Daboia russelli*), spectacled cobra (*Naja naja*), common krait (*Bungarus caeruleus*), and the saw-scaled viper (*Echis carinatus*). However, many other snakes of medical importance have been described over the years.^{1–5} In the Western Ghats of India, the malabar pit viper (MPV) (*Trimeresurus malabaricus*), bamboo pit viper (*Trimeresurus gramineus*), and large-scaled pit viper (*Trimeresurus macrolepis*), known *Trimeresurus* spp, are venomous and predominantly arboreal.⁴ No specific anti-snake venom (ASV) exists for these species in India.

MPV envenomation remains largely unreported from the Western Ghats and coastal regions of southwestern India. In a hospital-based registry from the hospital that treated this case, MPV envenomation was more common than *Echis*

carinatus and *Bungarus caeruleus* envenomation. We report a case with multiple bites to the face, potential upper airway obstruction due to severe cellulitis caused by the envenomation, coagulopathy caused by MPV, the potential neutralizing capacity of poly-specific Indian ASV in the treatment, and the role of thromboelastography in assessing the coagulopathy of MPV envenomation.

Case Report

A 44-y-old male, with no known comorbid conditions, from Honnavara, North Karnataka presented to the emergency department with swelling of the left side of the face after experiencing a snakebite while climbing a coconut tree at 1100. He was bitten twice, after which he immediately withdrew, killed the specimen, and presented to a local hospital where he was given tetanus immunization, diclofenac, and chlorpheniramine maleate and transferred to our hospital.

The patient arrived 6 h after the bite to the emergency department. The dead specimen was identified as an MPV (Figure 1) based on morphologic characteristics and the physician’s knowledge of species distribution in the region. On examination, he was conscious, oriented, and hemodynamically stable with a pulse rate

Corresponding author: Freston Marc Sirur, MD, Kasturba Medical College, Emergency Medicine, Manipal, Karnataka 576104, India; e-mail: sirur.freston@gmail.com; freston.sirur@manipal.edu.

Submitted for publication May 2021.

Accepted for publication October 2021.

Figure 1. (A, B) Killed specimen, identified as malabar pit viper (*Trimeresurus malabaricus*): green morph from Honnavara district-Near Sharavati, 14.2°N, 74.5°E. (C) Oral cavity of the specimen showing 2 fangs on the right with the left fang broken off. (D) Killed specimen. Full length of 57 cm with the typical black/brown spots over the dorsum arranged in a bold zig-zag pattern.

of 60 beats·min⁻¹, blood pressure of 120/70 mm Hg, hemoglobin oxygen saturation of 100% on room air, and respiratory rate of 18 breaths·min⁻¹. An airway

examination indicated no immediate threat to his airway. The local examination was painful with a diffuse swelling of the left cheek with multiple fang

Figure 2. (A) Fang marks: 2 sets of fang marks with 1 indistinct over the cheek. (B) Victim's face showing fang marks on the left cheek with edema extending to the neck.

Figure 3. (A) TEG at the time of admission showing a mild hypocoagulable state with primary hyperfibrinolysis. (B) TEG after 24 h showing a severe hypocoagulable state, probably due to fibrinogen deficiency and no fibrinolysis.

marks (Figure 2). Other systemic examinations were unremarkable.

A 20-min whole blood clotting test on admission was positive. A prothrombin time with international normalized ratio (PT-INR) was normal, and the thromboelastogram (TEG) revealed a mild hypocoagulable state with

primary fibrinolysis with a normal R time (Figure 3A). ASV was not started. He was admitted in the emergency intensive care unit for further evaluation and observation and because of the high possibility of the need for airway intervention. A serial PT-INR done 14 h after the bite was prolonged, and TEG revealed a hypocoagulable state

Table 1. Laboratory findings

	Reference range	6 h (Day 1)	18 h (Day 2)	22 h (Day 2)	42 h (Day 3)	66 h (Day 4)
Hb	13–17 g·dL ⁻¹	14	12	12	11	na
TLC	4–10 μ·L ⁻¹	9500	8800	na	4600	na
PLT	150–400×10 ³ μ·L ⁻¹	183×10 ³	177×10 ³	na	122×10 ³	119×10 ³
Urea	10–40 mg·dL ⁻¹	22	32	na	24	20
Cr	0.7–1.2 mg·dL ⁻¹	1.3	1.1	na	1.0	1.0
CPK	20–300 U·L ⁻¹	577	na	na	na	na
LDH	125–220 U·L ⁻¹	232	na	na	na	na
Urine pH	4.5–7.5	6.0	na	na	na	na
Protein	<30 mg·dL ⁻¹	30	na	na	na	na
Sugar	2–20 mg·dL ⁻¹	250	na	na	na	na
RBC	0–3/hpf	0.2	na	na	na	na
WBC	0–5/hpf	0.1	na	na	na	na

CPK, creatine phosphokinase; Cr, creatinine; Hb, hemoglobin; LDH, lactate dehydrogenase; na, not done/not available; PLT, platelet count (lakh); TLC, total leukocyte count; hpf, high power field.

Table 2. Coagulation parameters

	Reference range	6 h (Day 1)	14 h (Day 2)	35 h (Day 2)	43 h (Day 3)	67 h (Day 4)
20WBCT	20 min	Positive	na	Negative	na	na
PT	9.6–12.5 s	12.6	24.2	18.1	14.9	11.9
INR	Reference ranges as per Figure 3	1.2	2.3	1.7	1.4	1.1
aPTT	26.8–33.2 s	25.2	25.1	21.9	22.2	22.6
TEG		Mild hypocoagulable state	Hypocoagulable state			
		with primary fibrinolysis				

aPTT, activated partial thromboplastin time; INR, international normalized ratio; na, not done/not available; PT, prothrombin time; TEG, thromboelastography; 20WBCT, 20-min whole blood clotting test.

Figure 4. (A) Image of the opposite side of the face at the time of presentation. (B) Thermographic image of the bitten site showing lower temperature at the edematous area and higher temperature in the surrounding areas. (C) Image of the bitten side of face showing decrease in edema and swelling after ASV.

without hyper fibrinolysis (Figure 3B). He was also hypotensive with a blood pressure of 70/50 mm Hg. Ten vials of ASV (Bharath serums) were administered and a fluid bolus was given, to which he was found to be responsive. Intravenous amoxicillin-clavulanic acid, trypsin chymotrypsin, and paracetamol were given. A serial decline in platelets and hemoglobin was managed conservatively (Table 1). The elevated creatine kinase levels, serial serum creatinine, and urine analysis did not confirm renal injury. A peripheral smear done on Day 1 showed normal red blood cell morphology. He maintained normal urine output throughout the hospital stay. Serial PT-INR tests showed an improvement over the next 4 d (Table 2). Serial infrared thermography indicated a lower body surface temperature of the bitten cheek as compared to the left cheek and a normal temperature bilaterally on Day 3 (Figure 4). He did not develop any bleeding manifestations, renal injury, or airway compromise. He improved and was discharged on Day 4.

Discussion

The Western Ghats of India, one of 10 biodiversity hot-spots, span over 1600 km, from Gujarat to Kerala, with an average elevation of 1200 m and the highest peak being 2695 m above mean sea level. The area is host to a wide range of endemic species.⁶ The MPV is found in Maharashtra through Goa, Karnataka, and Kerala. It is arboreal, well camouflaged, and preys on amphibians and small reptiles.^{4,7} It is locally known as *happatte havu*. These bites are often unreported owing to the perception of their venom as being nonlethal.

Our patient was engaged in agricultural activity when he was bitten, after which he developed local edema that spread over the bitten half of his face and neck, impairing eye opening. In this situation, a potential airway compromise was anticipated; however, he maintained his airway and the edema subsided. Chymotrypsin and topical glycerin magnesium sulphate were applied, but it remains unclear as to how much benefit they offered in

resolution of symptoms. Venom ophthalmia is caused by ocular contamination with venom (eg, by spitting cobras),⁸ but facial bites by other venomous snakes may cause severe local envenomation and may secondarily compromise vision.⁹ There was no evidence of venom ophthalmia in this patient.

Embedded fang fragments may be retained and result in infection or ulceration and hence should be looked for using x-ray or ultrasound.¹⁰ In this case, ultrasound did not show evidence of the embedded fang.

Envenomation is mediated by phosphodiesterases, metalloproteinases, L-amino acid oxidases, and cysteine rich proteins, which may cause myonecrosis, hemolysis, platelet dysfunction, endothelial damage, and ion channel blockage.^{11,12} This patient's creatine phosphokinase, renal function, and electrolytes were monitored; creatine phosphokinase was elevated. His hemoglobin dropped from 14 g·dL⁻¹ on Day 1 to 11 g·dL⁻¹ on Day 4, but there was no apparent bleeding or hemolysis, as evidenced by the work-up. The only attributable causes were blood sampling for diagnostic testing, rehydration, and mild extravasation at the bite site. MPV venom, as compared to *Naja naja* and *Daboia russelli*, can cause severe local tissue degeneration.¹² Ion channel dysfunction and myonecrosis may cause electrolyte imbalances.

Infrared thermography has been studied and used as a diagnostic and monitoring tool in many situations,^{13,14} including local envenomation. The device used was an FLIR E8 camera with an image resolution of 320×240 pixels and a thermal sensitivity of <0.05°C (0.09°F)×<50 mK. Although there was a significant difference in temperature between the normal and the affected side, the temperature was actually lower around the bite site, which is attributed to the edema fluid and low ambient temperature.

The mild coagulopathy caused by MPV venom is primarily fibrinolytic, mediated by phosphodiesterases, metalloproteinases, and serine-protease like proteins such as malabarase.¹⁵ Although the patient had a positive 20 minute whole blood clotting test (MWBCT), the INR was only marginally elevated and TEG showed a mildly hypocoagulable state.¹⁶ MPV venom has potent thrombin-like enzyme (TLE).¹¹ TLE acts mostly on the alpha and to a lesser extent on the beta domain of fibrinogen, leading to consumption of fibrinogen without fibrin production. The fibrinogen consumption was evident from the first TEG; the graph showed evidence of ongoing clot lysis and decreased clot strength with normal clot initiation (normal R time). TEG assesses the coagulation cascade in clot initiation (R time), clot kinetics (K time and alpha angle), clot dynamics (maximum amplitude [MA], G and coagulation index), and clot resolution (Ly 30) and hence provides a clear picture of the dynamics of in vivo clot formation, unlike

PT or activated partial thromboplastin time (aPTT), which are static tests. The patient had signs of coagulopathy at the time of admission (Figure 3A), which later completely evolved into a severe hypocoagulable tracing in TEG because of the fibrinogen consumption by TLE (Figure 3b). The fibrinogen-fibrin-platelet crosslinking is traced by the parameters K time and alpha angle, whereas 80% of MA is contributed by platelets and the remainder by fibrinogen.¹⁷

K time and angle were in the normal or low normal range in TEG (3.4 and 51.7 min) and MA was slightly reduced (47.7 mm) at the time of admission, with a fibrinolysis value of (Ly30–45%) indicating fibrinogen consumption due to venom-induced consumptive coagulopathy (Figure 3a). The repeat TEG had revealed more evolved coagulopathy in terms of unrecorded K time and a severely reduced angle (16°) as well as MA (9.8 mm) without evidence of ongoing clot resolution, indicating that venom-induced consumptive coagulopathy had completely evolved by that time (Figure 3b).

A normal R time in TEG meant the clot initiation was normal, which was also evident from a normal PT and aPTT on admission. The hyperfibrinolysis could be attributed to the defibrination by the TLE. Coagulopathy by TLE affects fibrinogen; the early coagulation screen by PT or aPTT may be normal and might lead to unwarranted consumptive coagulopathy if left to evolve fully. The authors also believe that measuring fibrinogen levels in *Trimeresurus malabaricus* bites might prove beneficial in establishing early consumption, where viscoelastic tests are not available considering the Indian landscape and resources.¹⁸

ASV was initially withheld but, owing to the deranged coagulation profile the next day, 10 vials of Indian polyvalent ASV (Bharat Serums, Navi Mumbai, India) were administered. The ASV as per the manufacturer is only effective against the “big 4,” but there is some evidence of paraspecificity (Haffkine's,¹⁹ Virchow, and VINS¹¹). In vitro studies show the EC50 of ASV against MPV is significantly higher.¹¹

The patient was hypotensive on the first day but gradually improved on the second day. The 5' nucleotidase in the venom is a hypotensive agent.¹¹ As analgesia, nonsteroidal anti-inflammatory drugs such as diclofenac are often used, but caution is recommended because they are associated with platelet dysfunction, anaphylaxis, and renal injury.²⁰

Although species identification is important, it may also lead to complacency. It is therefore important to identify and recognize the possibility of life-threatening envenomation in pit vipers. *Trimeresurus malabaricus* also presents a challenge in identification owing to its shared habitat with other *Trimeresurus* species and its

varied morphologic features (at least 6 known color morphs). Syndromic identification is of limited value; therefore, there is a need for rapid diagnostic kits and species-specific/region-specific/pan-specific ASV.

Conclusions

We recommend that all *Trimeresurus* envenomations be considered medically significant. Thromboelastography is a useful tool for detecting and monitoring coagulopathy. The time to onset of systemic envenomation requires study, and the recommended period of observation should be modified accordingly. The role of Indian polyvalent ASV in these cases requires further in vitro and in vivo studies. Species identification is imperative for recognition of the burden and appropriate management of these cases. Research must focus on rapid diagnostic kits such as Dot-enzyme linked immunosorbent assay (DOT ELISA),²¹ and species-/pan-specific antivenom needs to be developed as early as possible.

Acknowledgments: We thank Nirmal Kulkarni for his guidance and support on studies on pit vipers in the Western Ghats.

Author Contributions: Original draft of manuscript, imaging of snake and bite site, identification of snake (FMS); drafting of manuscript, reviewing, and editing (VL); IR imaging (CAS); TEG analysis (GM); critical review of manuscript (SS); approval of the final manuscript (all authors).

Financial/Material Support: None.

Disclosures: None.

References

- Shivanthan M, Yudhishdran J, Navinan R, Rajapakse S. Hump-nosed viper bite: an important but under-recognized cause of systemic envenoming. *J Venom Anim Toxins Incl Trop Dis*. 2014;20:24.
- Simpson ID, Norris RL. Snakes of medical importance in India: is the concept of the “big 4” still relevant and useful? *Wilderness Environ Med*. 2007;18(1):2–9.
- Joseph JK, Simpson ID, Menon NCS, Jose MP, Kulkarni KJ, Raghavendra GB, et al. First authenticated cases of life-threatening envenoming by the hump-nosed pit viper (*Hypnale hypnale*) in India. *Trans R Soc Trop Med Hyg*. 2007;101(1):85–90.
- Whitaker R, Captain A. *Snakes of India-the Field Guide*. 2nd ed. Westland/Draco books; 2016:348–9.
- Mirza ZA, Bhosale HS, Phansalkar PU, Sawant M, Gowande GG, Patel H. A new species of green pit vipers of the genus *Trimeresurus* Lacépède, 1804 (Reptilia, Serpentes, Viperidae) from western Arunachal Pradesh, India. *Zoosyst Evol*. 2020;96(1):123–38.
- Chen A, Ng Y, Zhang E, Tian M. Western Ghats, India. In: *Dictionary of Geotourism*. Singapore: Springer; 2020:135.
- Sawant NS, Jadhav TD, Shyama SK. Distribution and abundance of pit vipers (Reptilia: Viperidae) along the Western Ghats of Goa, India. *J Threat Taxa*. 2010;2(10):1199–204.
- Lath NK, Patel MM. Treatment of snake venom ophthalmia. *Cent Afr J Med*. 1984;30(9):175–6.
- Chen CC, Yang CM, Hu FR, Lee YC. Penetrating ocular injury caused by venomous snakebite. *Am J Ophthalmol*. 2005;140(3):544–6.
- Kirwadi A, Pakala VB, Kumar DS, Evans PA. Tooth remnant in non-venomous snake bite on the face: a rare occurrence. *Emerg Med J*. 2008;25(11):782.
- Vanuopadath M, Shaji SK, Raveendran D, Nair BG, Nair SS. Delineating the venom toxin arsenal of Malabar pit viper (*Trimeresurus malabaricus*) from the Western Ghats of India and evaluating its immunological cross-reactivity and in vitro cytotoxicity. *Int J Biol Macromol*. 2020;148:1029–45.
- Gowda CDR, Rajesh R, Nataraju A, Dhananjaya BL, Raghupathi AR, Gowda TV, et al. Strong myotoxic activity of *Trimeresurus malabaricus* venom: role of metalloproteases. *Mol Cell Biochem*. 2006;282(1–2):147–55.
- de Medeiros CR, Brioschi ML, de Souza SN, Teixeira MJ. Infrared thermography to diagnose and manage venomous animal bites and stings. *Rev Soc Bras Med Trop*. 2017;50(2):260–4.
- Sabitha P, Bammigatti C, Deepanjali S, Suryanarayana BS, Kadiravan T. Point-of-care infrared thermal imaging for differentiating venomous snakebites from non-venomous and dry bites. *PLOS Negl Trop Dis*. 2021;15(2):e0008580.
- Kumar RV, Yariswamy M, Joshi V, Dharmappa KK, Venkatesha SH, Sharath BK, et al. Malabarase, a serine protease with anticoagulant activity from *Trimeresurus malabaricus* venom. *Comp Biochem Physiol B Biochem Mol Biol*. 2013;164(2):111–6.
- Ratnayake I, Shihana F, Dissanayake DM, Buckley NA, Maduwage K, Isbister GK. Performance of the 20-minute whole blood clotting test in detecting venom induced consumption coagulopathy from Russell’s viper (*Daboia russelii*) bites. *Thromb Haemost*. 2017;117(3):500–7.
- Carll T, Wool GD. Basic principles of viscoelastic testing. *Transfusion*. 2020;60(Suppl 6):S1–9.
- Berling I, Isbister GK. Hematologic effects and complications of snake envenoming. *Transfus Med Rev*. 2015;29(2):82–9.
- Warrell DA, ed. *Management of Snakebites*. 2nd ed. World Health Organization; 2016:128–9.
- Cannon CP, Curtis SP, FitzGerald GA, Krum H, Kaur A, Bolognese JA, et al. Cardiovascular outcomes with etoricoxib and diclofenac in patients with osteoarthritis and rheumatoid arthritis in the Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) programme: a randomised comparison. *Lancet*. 2006;368(9549):1771–81.
- Puzari U, Mukherjee AK. Recent developments in diagnostic tools and bioanalytical methods for analysis of snake venom: a critical review. *Anal Chim Acta*. 2020;1137:208–24.