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Case report

Severe and prolonged hypofibrinogenemia following *Protobothrops cornutus* snake bite: A case report from Vietnam



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ABSTRACT

We report a clinical case of severe and prolonged hypofibrinogenemia caused by envenomation from *Protobothrops cornutus*, an pit viper species found mainly in Vietnam and parts of southern China. A 60-year-old woman was bitten while hiking in Cuc Phuong national forest of Ninh Binh province, Vietnam. Although WHO guidelines discourage antivenom administration for minor coagulation abnormalities, in this case, the decision was made due to a fibrinogen level <1.0 g/l and the patient's risk factors, including age (60 years) and untreated arterial hypertension, increasing the risk of spontaneous cerebral hemorrhage. Her fibrinogen level progressively dropped from 1.5 g/l to a nadir of 0.24 g/l at 112 hours post-bite, despite administration of 60 vials of monovalent *Trimeresurus albolabris* antivenom (produced by the Institute of Vaccines and Medical Biologicals (IVAC), Nha Trang, Vietnam, and distributed by Vabiotech). A temporary increase to 1.13 g/l was observed after infusion of 400 ml of cryoprecipitate, but hypofibrinogenemia relapsed thereafter and only stabilized after 181 hours after *Protobothrops cornutus* bite. This clinical case highlights the distinctive coagulopathy caused by *Protobothrops cornutus* envenomation with severe and prolonged hypofibrinogenemia despite the use of large doses of monovalent *Trimeresurus albolabris* antivenom (which was not specific to *P. cornutus*) and cryoprecipitate while liver and kidney functions, creatine kinase (CK) levels, remained within normal limits, indicating that the venom primarily affected the coagulation system without causing damage to other major organs.

1. Introduction

Protobothrops cornutus, commonly referred to as the horned pit viper, is a rare venomous snake in Vietnam and parts of southern China, especially distributed in central regions such as Quang Binh, Quang Tri, and Thua Thien Hue province (Maduwage and Isbister, 2014; Kini, 2005). Like other pit vipers, this snake's venom contains substances that can speed up blood clotting in an abnormal way. This can lead to a range of blood-related problems, such as low fibrinogen levels, low platelet count, and conditions that resemble widespread abnormal clotting in the body (similar to disseminated intravascular coagulation) (Isbister, 2010; Mion et al., 2013). However, literature on clinical envenomation by *Protobothrops cornutus* remains sparse (see Table 1, Figs. 1 and 2).

Here, we present a clinical case of prolonged and severe coagulopathy following envenomation by *Protobothrops cornutus*, leading to the administration of large doses of monovalent *Trimeresurus albolabris* antivenom, which appeared ineffective in this case and cryoprecipitate

transfusion. This is among the first detailed clinical descriptions of coagulopathy due to this species at our poison control center in Bach mai hospital, Hanoi, Vietnam.

2. Case presentation

A 60-year-old woman with a known history of hypertension (non-compliant with medication) was bitten by a snake on the medial aspect of her left heel while hiking in Cuc Phuong national forest, Ninh Binh province, Vietnam, on June 5th, 2025. She captured the snake and brought it with her for identification. Local herpetologists later confirmed it as *Protobothrops cornutus*.

The bite occurred 1.5 hours before admission to Ninh Binh province general hospital, where the patient received analgesics and tetanus prophylaxis after that she was transferred to our Poison Control Center in Bach Mai hospital, Hanoi, Vietnam at 5 hours post-bite.

On admission.

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- Conscious, Glasgow Coma Score was 15, temperature was 37 °C and blood pressure was 140/90 mmHg, heart rate was 89 beat per minute.
- No mucosal or underskin bleeding.
- Localized pain was Visual Analog Scale (VAS) 6/10 with edema, swelling spreading 20 cm above the ankle,
- No neurotoxicity observed.
- Initial laboratory results were normal platelet count, light decreased fibrinogen (1.5 g/l), PT/APTT was slightly prolonged with PT is Prothrombin rate (%), not prothrombin time and APTT is activated partial thromboplastin time measured in seconds.

She was treated with intravenous clindamycin and oral paracetamol-codeine (500 mg every 6 hours). Clindamycin was initially used as empirical coverage for anaerobic and Gram-positive organisms; however, it is not the standard prophylactic choice for snakebites. Current guidelines discourage routine antibiotic use unless signs of infection are evident. Over the next 36 hours, edema, swelling and pain subsided. However, fibrinogen began decreasing gradually despite we infused antivenom therapy for patient.

At admission, INR was 1.1, PT was mildly prolonged to 14.7 sec (ref <13.5). Although the PT was 14.7 sec, the INR remained within normal limits (<1.2), suggesting normal coagulation based on standardized international measurement. According to WHO, these changes alone do not indicate the use of antivenom. However, in the clinical context of venomous *Protobothrops* envenomation, we considered early intervention necessary due to progressive hypofibrinogenemia. The total dose of antivenom administered was 60 vials of monovalent *Trimeresurus albolabris* antivenom together 400 ml of cryoprecipitate.

Liver function tests (AST, ALT), renal parameters (creatinine, urea), and CK levels were all within normal limits throughout hospitalization. Although other blood clotting tests and platelet counts returned to normal. However, the fibrinogen level stayed low until 8 days after the snakebite. The patient was not bleeding anywhere in body and finally she was fully recovered and discharged from our poison control center at 247 hours after snakebite with normal fibrinogen (2.19 g/l).

3. Discussion

This clinical case showed that the patient can present with severe and prolonged hypofibrinogenemia following envenomation by *Protobothrops cornutus*, a pit viper species endemic to Vietnam. Despite the early administration of a high dose of monovalent *Trimeresurus albolabris* antivenom with a total of 60 vials and the infusion of 400 ml of cryoprecipitate (Cryo) but the patient's fibrinogen levels remained critically low for a full 8-day post-bite. In addition, a mild drop in platelet count to 145 G/L was observed at 72 hours post-bite. This transient thrombocytopenia spontaneously resolved and is consistent with hematological patterns seen in *Trimeresurus* and *Calloselasma rhodostoma* envenomations in Southeast Asia and may reflect a shared pathophysiological response. This occurred even as other coagulation parameters gradually returned to normal, highlighting a unique pattern of isolated and prolonged hypofibrinogenemia. PT and APTT were not significantly disrupted and remained mostly within normal limits. These findings

Table 1
Changes of fibrinogen in patient's blood over time after snake bite.

Time post-bite snake(hours)	Hemoglobin (g/l)	Platelet (G/l)	INR	PT (%)	APTT (sec)	Fib(g/l)	Intervention
5	152	209	1.15	81	28	1.5	Admission
36	136	159	1.05	87	21	0.9	20 vials
72	124	145	1.05	78	21	0.5	40 vials
112	123	178	1.17	79	24	0.24	400 ml Cryo
124	117	175	1.02	97	23.9	1.13	After cryoprecipitate
156	122	227	1.28	70	24.8	0.4	Drop after temporary recovery
181	130	272	1.05	92	26	0.76	Progressive improvement
247	135	245	0.95	107	25.7	2.19	Discharge



Fig. 1. *Protobothrops cornutus* bites patient in Ninh Binh province, Vietnam.



Fig. 2. Image of patient's swollen leg when entering our poison control center (5th hour after snake bite).

support the hypothesis that *Protobothrops cornutus* venom exerts a strong coagulopathic effect through thrombin-like enzymes (TLEs), which catalyze the conversion of fibrinogen into non-clottable fibrin fragments. This process leads to a marked reduction in functional fibrin, thereby compromising effective clot formation and contributing to sustained hypofibrinogenemia. (Maduwage and Isbister, 2014; Kini, 2005). Unlike typical fibrin clots, these products cannot contribute to hemostasis, leading to persistent coagulopathy despite treatment. The relapse of hypofibrinogenemia observed after the initial Cryo support further implies ongoing venom activity or possible redistribution from a tissue depot, as has been proposed in other viper envenomations (Isbister, 2010; Mion et al., 2013). The transient improvement in fibrinogen levels appeared to be a response to cryoprecipitate rather than to antivenom administration.

Importantly, *Protobothrops cornutus* envenomation is rarely reported in the literature. This clinical case stands out as one of the first detailed clinical reports documenting its unique hematological toxicity, particularly its prolonged and the venom of *Protobothrops cornutus* appeared to exert predominant effects on fibrinogen levels, however, other coagulation factors were not evaluated in this case (Chen et al., 2009). Although prominent hypofibrinogenemia was observed in this case, similar patterns have been documented in other *Protobothrops* species and viperid bites (Lajoie et al., 2024). Previous reports of related species, such as *Protobothrops mucrosquamatus* cases were mild, others demonstrated severe complications including renal failure and myotoxicity (Lajoie et al., 2024). Thus, *Protobothrops* bites can present with a spectrum of severity (Chiang et al., 2020). Our findings also underscore the importance of extended fibrinogen monitoring well beyond the traditional 72-h observation window, especially in envenomations involving lesser-known or endemic species with uncharacterized venom profiles (Lavonas et al., 2011). Failure to do so may result in missed relapses and under-treatment, with potential risk for delayed bleeding complications. The patient exhibited a mild thrombocytopenia with a decrease in platelet count to 145 G/L at 72 hours, which resolved spontaneously and then returned to 245 G/l at discharge. Such thrombocytopenia is commonly reported following *pit viper* envenomations in Southeast Asia and likely represents a transient, venom-induced platelet consumption mechanism, further indicating that *Protobothrops cornutus* venom affects multiple components of the hemostatic system. Platelet count was normal at admission (209 G/l), slightly dropped to 145 G/l at 72h, and then returned to 245 G/l at discharge. Finally, this case raises concerns about the no observed cross-neutralisation by monovalent antivenom against *Trimeresurus albolabris*, as fibrinogen continued to drop despite 60 vials of administration of the currently available *Trimeresurus*-specific antivenom serum. Given the phylogenetic distance between *Protobothrops cornutus* and other *Trimeresurus* species, it is plausible that current antivenom serums lack sufficient antibody specificity against key *Protobothrops cornutus* venom components (Lavonas et al., 2011). There is a clear need for further research into species-specific venom composition and antivenom development to optimize treatment for rare but clinically significant envenomations such as this.

4. Conclusion

We wrote this clinical case to emphasize a characteristic that, some cases of *Protobothrops cornutus* envenomation can cause coagulation

disorder with a slight decrease in fibrinogen, but there are also special and rare clinical cases showing coagulation disorder with a severe and prolonged decrease in fibrinogen while the antivenom against *Trimeresurus albolabris* appears ineffective for *Protobothrops cornutus* envenomations. Therefore, clinicians need to must attention to this issue to better predict and treat patients with *Protobothrops cornutus* bites.

CRedit authorship contribution statement

Dang Duc Nguyen: Writing – review & editing, Writing – original draft, Supervision. **Nguyen Hong Anh Lam:** Methodology, Formal analysis. **Dang Bach Nguyen:** Software.

Ethic

This case report was conducted in accordance with the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments. Written informed consent was obtained from the patient for publication of the clinical details and accompanying images. All patient-identifying information has been anonymized to protect privacy.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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