Journal of the Postgraduate Institute of Medicine 2025; 12(1): E261 1-6
https://doi.org/10.4038/jpgim.8542

Case Report

Hump-nosed viper induced thrombotic thrombocytopenic purpura, prolonged AKI complicated by anterior STEMI

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Key words: **Hump nosed viper, thrombotic thrombocytopenic purpura, myocardial infarction, renal involvement**

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Received: 21 Sep 2024, Accepted revised version: 05 Jan 2025, Published: 25 Feb 2025

Competing Interests: Authors have declared that no competing interests exist

Introduction

Hump-nosed viper (HNV) bites are commonly encountered in the Sri Lankan setting. HNV bites elicit a plethora of reactions ranging from severe local cellulitis and necrosis to a range of hematological, renal and neurological complications. One such rare but important complication is thrombotic thrombocytopenic purpura (TTP). HNV bites trigger an acquired form of TTP. Involvement of the kidney and neurological system in TTP is widely described in the literature; however, cardiac involvement in TTP is uncommon. Though the exact prevalence of cardiovascular involvement in TTP is unknown, severe morbidity and mortality are reported in TTP patients with high levels of positive cardiac biomarkers. Management of a myocardial infarction (MI) in this setting is rather tricky and intricate due to ongoing acute kidney injury and low platelets as it impedes many therapeutic options for MI such as cardiac catheterization, treatment with dual antiplatelet therapy and percutaneous interventions. Yet we report a rare and challenging case of HNV bite leading to TTP and subsequently complicated by acute anterior STEMI.

Case presentation

A 63-year-old, previously healthy, male patient was transferred from the local hospital for further management of anuria even after undergoing 3 cycles of dialysis. The patient had had a snake bite 36 hours back, had not sought medical attention and presented to the local hospital with anuria and generalized body malaise. The snake was killed and brought to the hospital where it was identified as a hump nosed viper. On admission to the hospital, the patient was conscious, rational and oriented. A swelling was noted in the right fore hand. The patient was severely oliguric and ultimately became anuric over a few hours. Twenty minutes WBCT was clotted repeatedly. On examination the patient

was drowsy with marked pallor. His blood pressure was 160/94mmgh and he had a pulse rate of 100bpm. The results of the blood investigations are shown below (Table 1).

Table 1: Variation of hematological and biochemical parameters in the first 10 days following snake bite.

Parameter	**Day1 following snake bite**	**Day 5 following snake bite**	**Day 7 following snake bite**	**Day 9 following snake bite**	**Day 10 following snake bite**
White blood cells(*10^9/L)	16	12	13	6.7	8.1
Haemoglobin(g/dl)	8.5	7.2	7.0	8.9	8.2
Platelets/L	65000	15000	23000	50000	125000
C Reactive Protein	19	56	36	60	68
LDH(U/L)	1135	1155	2300	1129	678
Indirect bilirubin(µmol/l)	38.4	42.6	34	21	18
Direct bilirubin(µmol/l)	9.74	8.54	5.65	6.3	5.6
Retic Count	0.57%		3.7%		2.1%
Serum creatinine(µmol/l)	622.8	789	677	731	568
Prothrombin time/International normalizing ratio	1.18	1.2	1.13		0.94
APTT(sec)	31		32		34.1
Blood picture	Normochromic normocytic red blood cell, several fragments, bite cells, few polychromasia. Severe anemia with red blood cells changes suggestive of microangiopathic haemolytic anemia, marked thrombocytopenia with MAHA suggestive of venom induced TTP/DIC (figure 1)				

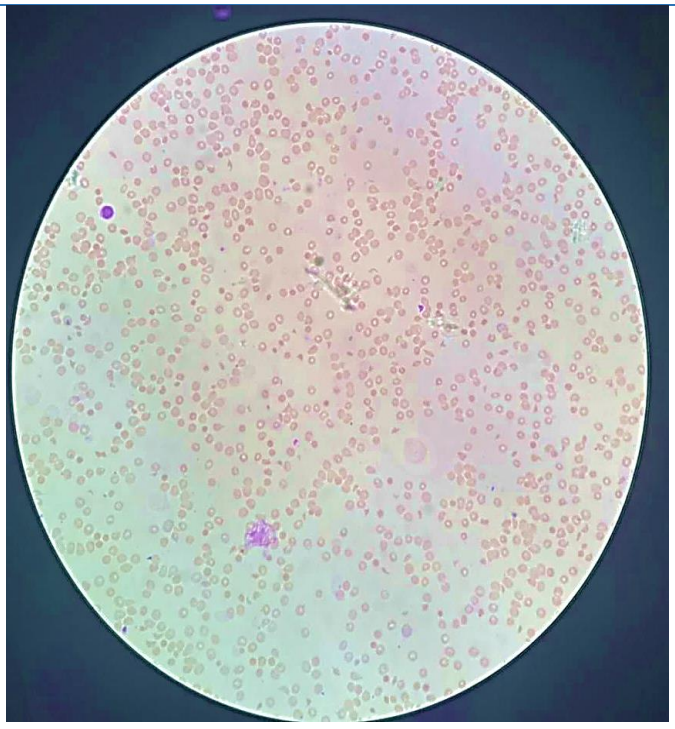

Figure 1: Blood picture showing schistocytes, bite cells, few polychromasia

The blood investigations showed evidence of haemolysis, thrombocytopenia, indirect hyperbilirubinaemia and impaired renal functions with a normal prothrombin time (PT)/international normalized ratio (INR) and activated partial thromboplastin time (APTT) level. With the above findings, TTP was considered the plausible event. The plasmic score of the patient was 7 which was interpreted as high risk. On day 2 of admission (5th day following snake bite) the patient started to become drowsy. The patient was started promptly on plasma exchange. His platelet rise was not satisfactory following first plasma exchange at only 23,000/L. Though repeated plasma exchange was indicated, the anuria hindered this, as he needed hemodialysis for anuria with acute kidney injury. Therefore, on the third day he underwent haemodialysis. On the fourth day, another therapeutic plasma exchange was done as daily blood pictures continued to show evidence of TTP. The patient underwent 3 cycles of plasma exchange but remained anuric throughout. Gradually the patient's conscious level normalized and his biochemical parameters such as LDH and indirect hyperbilirubinaemia started to show a subtle improvement. However, his LDH level was still above 1200. On ~~the~~ day 7 following the snake bite, he developed sudden onset shortness of breath and ~~a~~ chest pain. The ECG (which was obtained promptly showed anterior ST elevations (Figure 2).

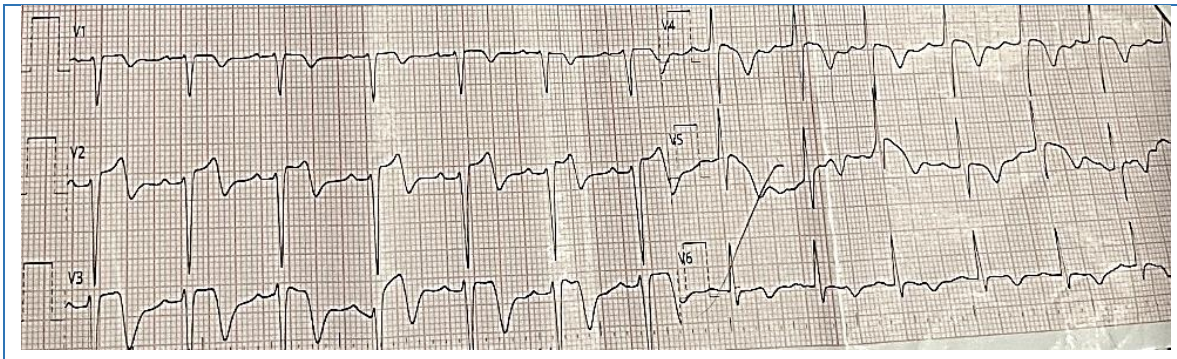

Figure 2: ECG showing anterior ST elevation MI with lateral T inversions.

Troponin I was recorded as 8.4ng/ml. It was decided to manage the STEMI conservatively as the patient's platelets were still low, though they had started to rise. Patient was started on atorvastatin 40mg during the acute stage and aspirin was commenced when platelet counts rose above 50,000/L. The 2D echo showed evidence of an anteroseptal apical MI with an ejection fraction of 35%-40%. Another hemodialysis and a plasma exchange cycle was done with much risk. The patient's platelet count started to rise following the fourth plasma exchange and his LDH level, indirect hyperbilirubinaemia and blood picture started showing a marked improvement. Ultimately, after 6 cycles of dialysis and 4 cycles of plasmapheresis his serum creatinine level gradually started to drop and he started producing urine. The patient's TTP status was monitored using LDH levels, indirect bilirubin levels and serial blood pictures. Table 1 shows the laboratory values over the course of the disease. The patient gradually improved and his shortness of breath resolved. When the platelet count~~s~~ rose above 100,000/L, he was started on enoxaparin 60mg daily which was continued for 5 days, while keeping a close eye on the platelet count and serum creatinine levels. On discharge, the patient was completely

asymptomatic with a platelet level of 170,000/L and serum creatinine of 200µmol/L. On a subsequent clinic visit after one week, the vascath was removed and his serum creatinine had normalized.

Discussion

Thrombotic thrombocytopenic purpura (TTP) is characterized by the concomitant occurrence of severe thrombocytopenia, microangiopathic hemolytic anemia (MAHA), and a variable degree of ischemic end organ damage. Formation of micro thrombi can cause extensive organ dysfunction [1,2]. The pathophysiology is elicited by micro thrombi forming in the arterioles and capillaries of multiple organs throughout the body. These thrombi are caused by systemic platelet activation and aggregation due to a failure of degradation of unfolded high molecular weight large von Willebrand factor (vWF), As a result, the patient may present with acute kidney injury, stroke, seizure, or myocardial infarction (MI) [2] The diagnosis of TTP may be confirmed by the demonstration of severe ADAMTS13 deficiency of <10%, But due to the limited availability of the test in Sri Lanka, clinical prediction scores for severe ADAMTS13 deficiency like the PLASMIC score and French score are used. In our patient, the plasmic score was 7 on admission.

The venom produced by the *Hypnale* has not been isolated and characterized but it is hypothesized that the procoagulant activity is due to thrombin-like enzymes (TLEs). TLEs activate clotting pathways leading to the formation of thrombi and deposit them as fibrin causing vascular occlusion. When red blood cells flow through these blocked vessels, they get distorted which can be seen on peripheral blood microscopy as schistocytes (fragmented red blood cells). This condition is called microangiopathic hemolysis and can be observed in *Hypnale* bites [3,4]. When organ ischemia occurs together with thrombocytopenia and microangiopathic hemolysis, the process is called thrombotic microangiopathy (TMA). Rathnayaka et al have described TMA following a hump-nosed viper bite which was successfully treated with multiple therapeutic plasma exchanges [4].Furthermore Withana et al highlight another case where a Sri Lankan woman developed TTP with fever, thrombocytopenia, microangiopathic hemolysis, renal impairment and neurological dysfunction in the form of confusion and coma five days after a *Hypnale* bite [5].

Cardiac involvement in TTP can present in the form of infarction, congestive heart failure, arrhythmias or cardiogenic shock. Although cardiac involvement in TTP is described in literature, the exact prevalence is still not determined. Prompt diagnosis and treatment is of paramount importance as mortality is significantly higher in patients with TTP who have cardiac involvement. Wiernek et al in a study on the cardiac implications of TTP highlight that an elevated cardiac troponin I is a reliable biomarker for cardiac involvement in TTP and recommend routine troponin measurement when a diagnosis of TTP is suspected or clinical deterioration is observed [6]. Furthermore, Patschan in his report has highlighted that acute myocardial infarction is an early, frequent and severe complication during TMA and states that a serum LDH above 1,000 U/l in combination with serum troponin I above 0.20 ng/ml at TMA presentation are excellent predictors of subsequent myocardial infarction [7]. In our case, the LDH level was above 1000, when he developed with acute MI.

In our patient, MI developed on the 7th day following the snake bite and his diagnosis was supported by a history of acute onset retrosternal chest pain, electrocardiographic changes, and a raised troponin I titer and 2D echo findings. In such a setting, where the patient has acute renal failure with high serum creatinine levels, changes in troponin titers need to be interpreted with caution since abnormal renal function per se could lead to a raised titer. Our patient's troponin I showed serial elevation at 8ng/ml, 13ng/ml and 25ng/ml respectively. The presence of regional wall motion abnormalities on an echocardiogram corresponding to the electrocardiographic changes was also supportive of a myocardial infarction. In a man aged 63 years, the possibility of pre-existing atheromatous disease cannot be excluded. But the fact that he was free from common, major identifiable risk factors such as diabetes mellitus, hypertension, hyperlipidemia and tobacco smoking deemed it unlikely. During the time that our patient developed myocardial infarction his blood pressure was recorded as normal with a normal hemodynamic status. There were no episodes of hypotension during the dialysis performed the previous day and the serum electrolytes done on the same day were within normal limits.

Our case report highlights the well-known sequel of TMA following hump-nosed viper bite and the relatively rare phenomenon of an acute ischemic event, as a consequence of TTP. Due to its rarity, the consensus regarding the exact management of patients with TTP-induced MI is lacking. The management was rather complicated and challenging. De Silva NL has reported a fatal case of hump-nosed viper bite complicated by TTP and non-ST elevation myocardial infarction [8]. In contrast, our case reports a TTP complicated with a STEMI which was successfully managed in the ward setting without ICU care.

Our experience in managing this patient provides the first case report of a STEMI in a patient with TMA following a hump-nosed viper bite. Sri Lankan physicians will continue to encounter hump-nosed viper bites more frequentl, and the management principles adopted in this case will guide medical teams in the future.

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