Case Report

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Thrombotic microangiopathy following saw-scaled viper (*Echis carinatus*) envenoming in Sri Lanka

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Abstract

The saw-scaled viper (*Echis carinatus*) is considered as a highly venomous snake in Sri Lanka. The clinical manifestations are localized pain and swelling, coagulopathy and renal impairment. Thrombotic microangiopathy is rarely reported as a complication of saw-scaled viper envenoming. The clinical manifestations of thrombotic microangiopathy include thrombocytopenia, microangiopathic haemolytic anaemia and acute kidney injury. The consumption coagulopathy of post-envenoming could be followed by a syndrome consistent with thrombotic microangiopathy. We describe a patient with thrombotic microangiopathy following saw-scaled viper systemic envenoming which was managed with antivenom and supportive therapy. The dead snake which was brought by patient was identified by medical professional as saw-scaled viper (*E. carinatus*) based on morphological features. This case illustrates a rare manifestation thrombotic microangiopathy following saw-scaled viper envenoming.

Keywords

Saw-scaled viper, thrombotic microangiopathy, thrombocytopenia, microangiopathic haemolytic anaemia, acute kidney injury

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Introduction

The saw-scaled viper (SSV) (*Echis carinatus*) is one of the highly venomous snakes in Sri Lanka.[1,2] The clinical manifestations of SSV bites are not well-described in the literature due to rarity of distribution in Sri Lanka.[1,2] The reported clinical manifestations include local effects, coagulopathy, renal impairment and myocardial ischaemia.[1–5] Thrombotic microangiopathy (TMA) is extremely rarely reported following SSV envenoming in the literature.[6] The presence of thrombocytopenia, microangiopathic haemolytic anaemia and acute kidney injury (AKI) favours the diagnosis of TMA[7,8] which may co-exist with venom-induced consumption coagulopathy (VICC) or after resolution of VICC.[9] The overlap between TMA and VICC is common reason for mistaken idea that snake bites cause disseminated intravascular coagulation. We describe a patient with TMA following SSV systemic envenoming in Northern Sri Lanka which was managed with antivenom and supportive therapy. The dead snake which was brought by patient was identified by medical professional and was confirmed by herpetologist as SSV (*E. carinatus*) (Figure 1).

Case history

A 55-year-old healthy female was admitted to medical unit with a history of local pain and swelling of right hand following a saw-scald viper bite. The dead snake which was brought by patient was identified by herpetologist as SSV (*E. carinatus*) (Figure 1). On examination, she had local swelling and fang mark at bite site. Her vital signs were stable. She had no signs of systemic envenoming at time of admission. Her 20-min whole blood clotting test (WBCT) showed incoagulable blood. Her blood investigations were shown in Table 1. Her clotting profile including international normalized ratio was more than 12 and activated partial thromboplastin time was more than 128 s, respectively. Her electrocardiogram was normal. She was initially managed with intravenous administration of 10 vials of Indian

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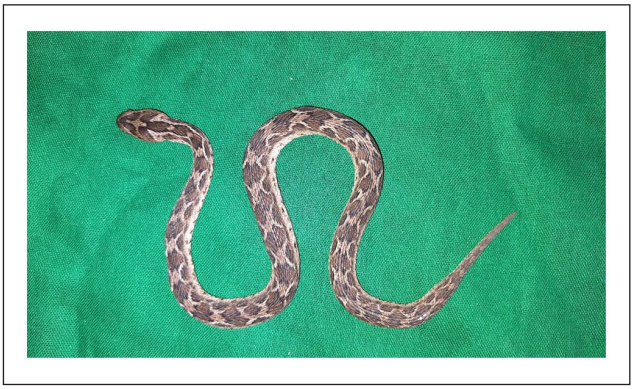

Figure 1. The dead specimen of saw-scaled viper (SSV) (*Echis carinatus*) which was brought by patient.

polyvalent antisanke venom (AVS, Batch No.: A05320055) along with intravenous hydrocortisone 200 mg and intravenous chlorpheniramine 10 mg. The repeated 20-min WBCT at 6 h showed incoagulable blood. Therefore, 10 vials of AVS were repeated along with intravenous hydrocortisone 200 mg and intravenous chlorpheniramine 10 mg.

Twelve hours after her admission, her laboratory investigations showed serum creatinine level of 2.1 mg/dL with ultrasonic evidence of AKI. Twenty-four hours after her admission, her laboratory investigations showed a drop in haemoglobin to 10 g/dL and platelets of 131 × 103/μL with an elevated total bilirubin of 1.9 mg/dL. Her serum lactate dehydrogenase level was 850 U/L (240–480 U/L) and reticulocyte count was 4%. Her liver enzymes and coagulation profile were normal. Her blood film showed normochromic normocytic anaemia, marked thrombocytopenia and fragmented red blood cells (schistocytes) which was suggestive of microangiopathic haemolytic anaemia (MAHA). Her further investigations were shown in Table 1. Her general condition was stable without other systemic neurological or respiratory compromise. With the presence of acute renal failure, thrombocytopenia and intravascular haemolysis with normal clotting profile, the diagnosis of TMA was made. She was closely monitored for clinical and biochemical deterioration of renal function. Her urine output was maintained 1–1.5 mL/kg/h with intravenous normal saline 100 mL/hourly for 72 h and intravenous furosemide 40 mg twice daily for 72 h. Her renal function was gradually recovered and repeated blood investigations revealed no evidence of haemolysis. She had no any residual renal impairment and her peripheral blood film showed no any other abnormalities at her clinic visit.

Discussion

The SSV is one of the highly venomous snakes in Sri Lanka. They are limited to certain parts of dry zones of Sri Lanka, especially in Northern Province of Sri Lanka.[1,2] The clinical manifestations of SSV bites are not well-described in the literature due to rarity of distribution in Sri Lanka. The local envenoming, AKI, myocardial infarction and haematological manifestations such as thrombocytopenia and haemolytic anaemia were reported following SSV bites.[1–5] The exact pathophysiology of clinical manifestations are not well-known. The venom contains many toxic compounds which activate to cause derangement in hemostasis such as platelet aggregation inhibitors, carinatin, ecHertatin, and echicetin, protein C activator, fibrinogenolysin, calcium-dependent carinactivase and disintegrins.[10] The pain, swelling and necrosis are due to phospholipase A2 component and spontaneous bleeding is due to activation of prothrombin by metalloproteinase.[11] The VICC occurs due to activation of clotting system by procoagulant enzymes in SSV venom. They can cause hypofibrinogenemia and disseminated intravascular coagulation resulting multi-organ dysfunction and death.[12] However, the venom profiles differ from other geographically distinct venoms of *E. carinatus* due to change in the relative composition of the toxin families.[13] Snake venom metalloproteinase, snaclecs and phospholipase A2 are the major venom components in all the venoms.

TMA is a rare complication of snake envenoming associated with subsets of snake bite patients with VICC. It is characterized by MAHA, AKI and thrombocytopenia.[14,15] The VICC is most common complication haemotoxin-induced coagulopathy, characterized by prolonged clotting profile, hypofibrinogenemia and a raised D-dimmer level.[9,14,16] The rapid onset and resolution of coagulopathy within 48 h, absence of systemic microthrombi and end organ damage in VICC usually differentiates from DIC.[9,14] TMA can occur after resolution of VICC or may overlap with VICC.[9,17–19] The overlapping between TMA and VICC is likely reason that snake bite causes DIC.[9] Many case reports described that TMA occurs overlapping with VICC or after resolution of VICC. Here, we describe a patient with MAHA and AKI suggestive of TMA after resolution of VICC following SSV systemic envenoming. In our patient, VICC settled within 24 h with antivenom therapy. Subsequently, she developed AKI, thrombocytopenia and MAHA which made a diagnosis of TMA.

The TMA syndromes are group of disorders with the unifying pathognomonic hallmark of vascular small vessel damage with microthrombosis.[7,20] This is characterized MAHA with fragmented red cells which manifests as haemolysis with circulating schistocytes on examination of blood film.[8,21] The presence of thrombocytopenia and MAHA is sufficient for diagnosis for TMA.[8,20] Furthermore, evidence of haemolysis such as anaemia, raised lactate dehydrogenase and unconjugated hyperbilirubinemia and lowered haptoglobin are nonspecific supportive for diagnosis of TMA. The diagnosis of TMA was confirmed in our patient with the presence of thrombocytopenia, MAHA and AKI. The vaso-occlusive end organ injury is causative for multi-organ dysfunction in TMA[21] and is due to an immune-mediated deficiency of a disintegrin and metalloproteinase with a

Table 1. The investigation profile of patient is shown with clinical progression of disease.

Investigation profile	Day						
	Admission	12 h	24 h	Day 2	Day 3	Day 5	Day 7
Complete blood count							
White cell count (4000–11,000/mm^3)	14,800	13,800	12,000	14,000	12,000	11,000	6840
Neutrophils (50%–70%)	50	89	80	74	70	72	56
Lymphocytes (20%–40%)	37	4	14	10	19	19	36
Haemoglobin (12–16 g/dL)	13.7	12.0	10.0	10.0	10.4	12.0	13.1
MCV (80–100 fL)	78	84	91	90	90	89	86
Red cell count (400,000–550,00 mm^3)	480,000	400,000	341,000	310,000	307,000	334,000	410,000
Platelets (150,000–450,000 mm^3)	287,000	154,000	131,000	92,000	130,000	145,000	210,000
Renal functions tests							
Blood urea (18–55 mg/dL)	44	55	75	60	55	45	32
Serum creatinine (0.7–1.5 mg/dL)	1.2	2.1	3.1	2.7	1.8	1.7	1.1
Serum electrolytes							
Serum sodium (135–145 mmol/L)	135	135	138	138	134	137	135
Serum potassium (3.5–5.0 mmol/L)	4.1	4.7	5.1	5.6	4.8	4.2	3.9
Liver profile							
Serum AST (0–45 U/L)	24	48	54	72	60	48	40
Serum ALT (0–35 U/L)	28	40	48	58	42	34	38
Total bilirubin (0–2.0 mg/dL)	1.1	1.8	2.8	2.4	1.5	1.3	1.0
Indirect bilirubin (0–1.6 mg/dL)	0.8	1.2	1.9	1.8	0.9	0.8	0.8
Clotting profile							
PT/INR (<1.4)	>12	1.2	1.2	1.0	1.1		1.2
APTT (<35 s)	>128	32	32	34	32		35
Urine full report	Nil	–	Nil	–	–		Nil
Protein (+)	1.2	–	3–4	–	–		3–5
Pus cells (/HPF)	10–15	–	5–10	–	–		5–10
Red cells (/HPF)	Nil	_	Nil	–			Nil
Active sediment (+)							
Serum CPK level	–	1051	–	325	–	243	109

MCV: Mean Corpuscular Volume; AST: Asparate transaminase; ALT: Alanine transaminase; PT/INR: Prothrombin time/International normalized Ratio; HPF: High PowerField; CPK: Creatinine Phosphokinase.

thrombospondin type-1 motif, member 13 (ADAMTS-13).[20] TMA associated with snake bites such as hump-nosed pit viper (Genus: *Hypnale*), Russell's viper (*Daboia russelii*), lowland viper (*Proatheris superciliaris*), Australian brown snake (*Pseudonaja*) and coastal taipan snake (*Oxyuranus*) and Saharan horned viper (*Cerastes cerastes*) has been described in the literature.[17,22–26]

Plasma exchange has a role in the treatment of TMA following snake bite. It decreases the further endothelial damage of blood vessels and normalizes the coagulation cascade and platelet aggregation via removal of toxins from blood.[27] Snake bite–associated TMA with AKI has improved with plasmapheresis treatment with normalization of renal function in published case reports.[28,29] In some other case reports of snake bite–associated TMA with AKI that the renal end organ damage resolves with renal replacement alone.[19] Other studies report that the renal end organ damage is self-limiting. However, plasma exchange in the management of TMA post-envenoming is a matter of debate. Furthermore, plasmapheresis has been used in some studies with perceived benefit. Our patient did not undergo plasmapheresis following SSV envenoming.

The ADAMTS13 cleaves the large von Willebrand factor which inhibits spontaneous bleeding and platelet aggregation. When ADAMTS13 is normal, plasmapheresis has no beneficial effect in the management of snake envenoming causing TMA.[9] This may be the reason for improvement of biochemical and renal function of our patient with antivenom and supportive therapy alone.

Conclusion

This case illustrates rare manifestation TMA following SSV bite which was managed with antivenom and supportive therapy in Northern Sri Lanka.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual case reports.

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Informed written consent

The informed written consent was obtained from patient to publish this case report.

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