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Case Report
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Rare Manifestation of Thrombotic Microangiopathy and AKI Following Russell's Viper Bite: A Case Report in North India

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ABSTRACT

Serious health issues are brought on by snake bites, in rural India. In 5-30% of instances, acute kidney injury (AKI) happens. One of the most prevalent and significant systemic clinical disorders is coagulopathy, which can become worse when there is an important and potentially fatal bleeding episode. Venom-induced consumption coagulopathy (VICC) is the most prevalent coagulopathy following snakebite and is caused by envenoming Viperid snakes and some elapids. Depending on the specific procoagulant toxin present, procoagulant toxins can activate the clotting pathway and result in a wide range of factor shortages. Therefore, the venom activates vital coagulation factors, and when they are depleted, coagulopathy sets in. Thrombotic microangiopathy occurs in a portion of VICC patients (TMA). This report examines a clinical scenario of TMA linked to snakebite, including its aetiology, diagnosis, treatment, results and response to antivenom and therapeutic hemodialysis. Acute kidney damage (AKI) spectrum, thrombocytopenia in nearly all instances and microangiopathic hemolytic anaemia (seen by schistocytes on the blood film) are the clinical manifestations of snakebite-associated TMA. Although there is no proof that antivenom specifically prevents TMA, the cornerstone of treatment for snake envenoming is still early antivenom. Patients should have long-term follow-up since they are at risk for developing chronic renal disease.

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Key Words
Thrombotic microangiopathy, snakebite, acute kidney injury

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INTRODUCTION

A snake bite causes 45,900 deaths annually and 3% of all cases are of acute kidney injuries (AKI) reported in India. AKI impedes the course of a viper bite in 5-30% of cases[1]. Snakebite-related Thrombotic Microangiopathy (TMA) is characterised by thrombocytopenia, microangiopathic hemolytic anaemia and acute kidney injury (AKI)[2]. Studies described TMA due to Viperidae bites by Daboia Russell (Russell's vipers) in India and Sri Lanka[3-4]. Snakebite-associated thrombotic microangiopathy (TMA) appears to be uniquely linked to predominant acute kidney injury (AKI), as was seen in this case report, which is a rare presentation following proven Rusells's viper bites manifested with AKI with a transient VICC for 6 hours, that has very less literature showing TMA associated with snake bites.

This study aimed to report the first case from North India of TMA and AKI with transient VICC following Russell's viper snakebite envenomation (Viperidae family), highlighting current studies from a perspective of clinical application.

Case Presentation:

Case Reports: A 11 year old boy, presented to us with an alleged history of a snake bite (Russells's viper) over his right foot. There was no history of nausea, vomiting, drowsiness, bleeding from any other site, abdominal pain, or any significant past history related to any bleeding disorders. On examination, he had pallor, was icteric and had localised edema of the affected leg as shown in Figure 1.

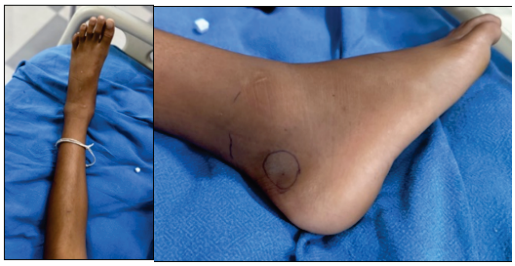

Fig. 1: Pallor and Icteric and Localised Edema of the Affected by

The anamnesis revealed that the snake was a Rusells's Viper (Daboia Russelli), as shown in Figure 2.

Fig. 2: RU Sells's Viper (laboia Rusclli)

Upon physical examination, the patient was euglycemic and normotensive. Results of his general examination were normal; however, the local examination showed signs of edema and erythema around the bite mark site of the dorsal aspect of the right foot 3 cm above the ankle, as shown in the figure. Vitals and system examinations were normal. Initial laboratory findings, including a complete blood count, liver and renal function tests, an electrolyte panel, has been charged in the given table from the day of snake bite.

Electrocardiography and chest X-ray were also normal. Hemostatic parameters initially revealed prolonged WBCT. Viral markers, chest X-ray and electrocardiogram were normal. Ultrasound showed normal sized kidneys with increased echogenicity and normal corticomedullary differentiation. Thrombotic microangiopathy secondary to snake bite envenomation was considered a cause of AKI Stage 3. Antivenom was administered as soon as patient was received in emergency and high dose intermittent bolus therapy was given, according to QRG guidelines of MoHFW, following one episode of haematuria and non clotted WBCT.

Owing to the additional presence of schistocytes on peripheral blood smear and thrombocytopenia 48 hours following the snakebite a diagnosis of snakebite-induced TMA was also made. Ultrasound scan revealed features of bilateral acute parenchymal renal changes, confirmed with laboratory findings on day 4 and the patient was started on haemodialysis for oliguric acute kidney injury and fluid overload on day 5 of the bite. He underwent five sessions of hemodialysis on alternate days. His local swelling started to subside on day 5. His blood parameters and urine output improved eventually after serial haemodialysis around 8 days from the bite and he was discharged on a Nephrology follow-up on day 14 of the P-ICU stay, with serum creatinine value of 4.5 mg/dL and urine output of 2.0 cc/kg/hr. He was kept on weekly nephrology follow up for follow up of ESRD.

RESULTS AND DISCUSSION

The majority of Indian patients with AKI are victims of saw-scaled and Russell vipers. It is still unclear how TMA works in cases of snakebite. Toxins in the venom, however, are thought to be the potential source of fibrin microthrombi deposition and endothelial damage[5] that lead to TMA. The path mechanism of venom-mediated endothelial damage includes activation of the alternative complement pathway, DIC, and TMA, which can result in patchy or diffuse cortical necrosis. AKI, thrombocytopenia, and microangiopathic hemolytic anaemia (MAHA) are clinical signs of hemolytic uremic syndrome (HUS)[3], which is comparable to the clinical picture of thrombotic microangiopathy. TMA in snakebite may occur without

Table 1: Parameters and Days Evaluation

Parameters	Day 1	Day 3	Day 8	Day 11	Day 14
Hemoglobin (RV:13,5-17g/dL)	12.5	8.4	9.0	9.5	9.5
RBC COUNT	4.3	3.14	3.50	3.52	3.60
MCV	85	74.2	84	85	87
MCH	27	26.6	28	27	28
MCHC	36.2	35.9	35.6	36	37
White blood cells (RV:3.600-10.000/µL)	6500	10,100	6000	10,000	7500
Platelets (x103/mm3) (RV:150.000-450.000/mm3)	2,00,000	15000	8000	3,00,000	1,50,000
PT (RV: <14 seg) a PTT (RV: < 28 seg) INR (RV: <1,2)	Non CLOT	17.3 76.3 1.34 76.3	Normal	Normal	Normal
Fragmented cells in PBF	Not Present	Numerous	FEW	FEW	Not Present
Sodium (RV: 135-148 mmol/L)	141	143	144	136	139
Potassium (RV: 3,5-5,3 mEq/L)	4.6	4.7	4.2	4.6	4..4
Calcium	9.7	8.4	8.6	8.9	9.0
Phosphorus	4.3	4.6	3.9	6.0	4.6
Serum Uric acid	2.3	8.3	3.5	3.6	3.9
Creatinine (RV: 0,7-1,3 mg/dL)	1.1	3.2	4.3	8.3	4.1
Urea (RV: 13-43mg/dL)	29	157	198	322	173
Urine PROTEIN	Nil	Nil	3+	3+	2+
Urine RBC	Nil	Numerous	Numerous	Numerous	FEW
LDH (RV: 230-460U/L)	693	1463	2556	3662	724
CPK (RV: < 195U/L)	582	631	893	901	60
SGOT (RV: < 38U/L)	83	140	172	59	40
SGPT (RV: < 41U/L)	35	40	55	40	42
Total bilirubin (RV: = 1,0 mg/dL)	0.6	2.0	3.0	2.2	0.6
Indirect bilirubin (RV: = 0,8 mg/dL)	0.2	0.2	0.2	0.4	0.1
Urine for Haemoglobinuria	-	Present	Present	Present	Absent

venom-induced consumption coagulopathy (VICC), as was uniquely seen in our case report, even though numerous studies have documented this relationship[6-7]. Prothrombin, thrombin-like enzymes, and factor X activators found in VICC activate the coagulation cascade, resulting in longer clotting times, the venom[4-8], which resolves after the toxins neutralisation. Coagulopathy in snakebite has historically been referred to as DIC because it provides a more compelling explanation for the clinical characteristics of DIC, and the absence of other abnormalities, venom-induced consumption coagulopathy, or VICC, has been described recently. Microvascular thrombotic blockage, nonrenal end-organ failure, and bleeding without visible fibrin deposition are the hallmarks of VICC, which is caused by the action of snake toxin in the coagulation pathway rather than the tissue factor/factor VIIa pathway. Prothrombin, factor X activators and thrombin-like enzymes in the venom activate the coagulation cascade, which results in prolonged clotting periods in VICC. TMA affects a subset of patients who have been envenomated by a snake bite, whether or not they have VICC. According to the suggested mechanism, venom or its vascular endothelial toxins may cause endothelial damage to induce TMA by acting as von Willebr and factor activators or vascular endothelial growth factor-type factors.

Regarding the management of TMA related to snakebite envenoming, there are disagreements. Treatments for snakebite-induced TMA[3] include supportive care, hemodialysis, plasma exchange, and antivenom injection. Typically, only antivenom seems to alleviate TMA linked to VICC when the toxins in snake venom are neutralised[7]. After the second day following the bite, the current case experienced a delayed period of thrombocytopenia with the lowest platelet count.

Fibrin microthrombi deposition is the likely mechanism behind acute kidney injury resulting from snakebite-associated thrombotic microangiopathy, as indicated by histological investigations published in the literature[5-9-11] Within the first 48 hours after the bite, our patient experienced a fast and progressive acute kidney injury (AKI), accompanied by rising serum creatinine levels and falling estimated glomerular filtration rates. Additional mechanisms of AKI in snakebite include the venom's direct effect on the kidney as well as the inflammatory responses brought on by the release of various endogenous cytokines and mediators[12].

We report a patient who developed TMA after being bitten by Russell's viper. For renal TMA, he underwent antivenom treatment and haemodialysis. A total of five cycles of dialysis therapy were received and an improvement in blood parameters and urine output

was seen. The patient has been kept on regular follow-up to see the development of CKD. In conclusion, TMA[8] should be taken into consideration in patients who have had a snake bite and who also exhibit AKI, thrombocytopenia, MAHA and a normal coagulation profile, as was seen for our patient. The renal prognosis may be improved by an early diagnosis, plasmapheresis and dialysis.

The two main recommended treatments for TMA after snakebites are renal replacement therapy (RRT) and plasma exchange, provided appropriate antivenom is administered[8-11]. A general treatment for various toxicological illnesses that quickly eliminate toxins from the bloodstream is plasmapheresis. It is currently unclear, though, how well this therapy works to cure TMA brought on by snakebite[8]. When existing medical therapy is ineffective in treating potentially fatal abnormalities in fluid, electrolyte, or acid-base balance, RRT should be started.

CONCLUSIONS

The first documented case of a Russells's viper bite that progressed to TMA in North India is described in this paper. There was no need for plasma exchange or red blood cell transfusions because the conservative treatment worked. Following TMA, severe AKI developed, for which Hemodialysis was done, along with a partial return of renal function. It is improper to refer to snakebite as TTP and HUS. While it is different from both TTP and HUS, snakebite is a disease that is linked to secondary TMA and the term "TMA associated with snakebite" is favoured. It is advised to define snakebite-associated TMA as having either thrombocytopenia (platelets <150 × 109/L) or a >25% drop in platelets from baseline, in addition to MAHA with ≥1.0% schistocytes. Early intervention with antivenom at the earliest indication of envenoming continues to be the standard of care for snakebites, notwithstanding the lack of data supporting antivenom's involvement in the prevention of TMA in patients presenting with VICC.

Patients with TMA are susceptible to CKD after their initial recovery, just as those with other causes of AKI, hence, long-term follow-up is highly advised. This should involve keeping an eye on renal function, managing or avoiding additional renal risk factors, and managing chronic kidney disease (CKD) as needed.

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