Case Report

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Snake Bite Presenting as Haemolytic Uremic Syndrome: A Rare Case Report

Internal Medicine Section

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ABSTRACT

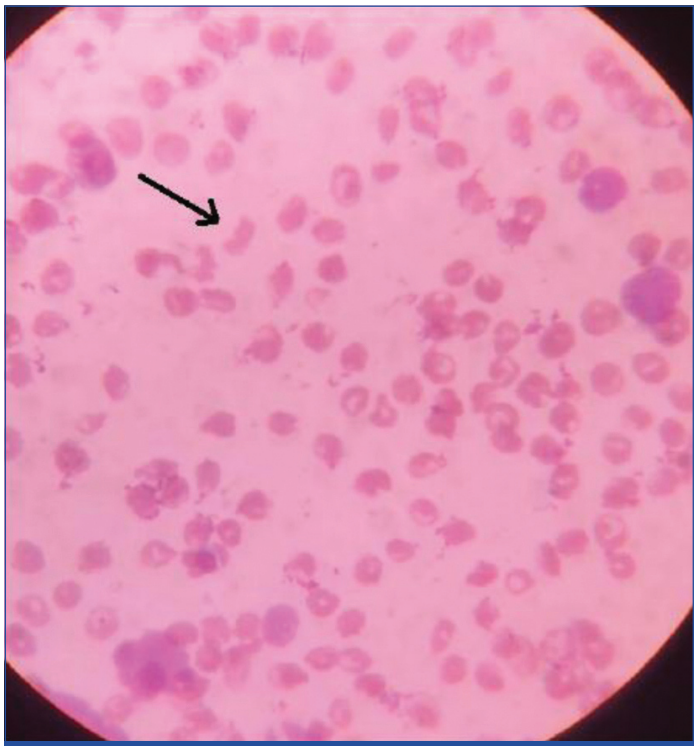
Snake bite is predominantly an occupational hazard and causes severe health issues. Snake poisoning in India is a significant and prevalent cause of Acute Kidney Injury (AKI). In India, the occurrence of AKI after snake bite is 13-32%. All over the world every year, 1,50,000 people die as a result of it. Multiple mechanisms such as haemodynamic disturbances, direct tubular toxicity, coagulopathy, haemoglobinuria, and myoglobinuria can cause AKI after bites by snakes belonging to the Elapidae, Viperidae, and Colubridae families. Renal pathologic findings include acute tubular necrosis, cortical necrosis, interstitial nephritis, glomerulonephritis, and vasculitis. Thrombotic Microangiopathy (TMA) as a cause of snakebite-induced AKI is rarely reported in literature. Fewer details are known about the clinical course, optimal management, and overall prognosis of this entity. Haemolytic Uremic Syndrome (HUS) is a clinical disease that includes TMA, thrombocytopenia, and AKI as a triad. The HUS is a heterogeneity of illnesses with diverse aetiology which results in presentation, therapy and outcomes variance. Hereby, authors report a case of a 55-year-old female who was bitten by Russell's viper and developed HUS. Patient eventually progressed to end stage renal disease and was advised lifelong haemodialysis. TMA should be taken into account as a probable cause of AKI following a snake bite. Plasma exchanges have yet to be determined in snake bite TMA.

Keywords: Acute tubular necrosis, Microangiopathic haemolytic anaemia, Russell's viper, Thrombotic microangiopathy, Thrombocytopenia

CASE REPORT

A 55-year-old female, farmer by occupation presented to casualty with alleged history of snake bite three and half hours back on her right foot while working in the field. The patient's co-worker identified the snake as Russell's viper, but the snake was not captured. There was immediate local swelling noted by the patient and after approximately 20 minutes the patient started to have multiple episodes of vomitings and abdominal cramps. She then came to the Out Patient Department (OPD) of this hospital. On examination, two fang marks were present, patient had swelling over local site along with erythema aproximataly 6×3×5 cm, raised local temperature and marked tenderness. Pulse was 120/minute, regular Blood Pressure (BP)-168/96 mmHg in right arm. Vitals and system examinations were normal. There was no neurodeficit noted. On admission investigations revealed, Haemoglobin (Hb) 14.5 gm%, Total Leukocyte Count (TLC) 27400/mm^3, platelet count 68,000/mm^3, serum creatinine 1.2 mg%, urea 44 mg%, sodium 141 mEq/L, potassium 4.3 mEq/L. Coagulation profile and Liver Function Test (LFT) was within normal limits. There was no evidence of schistocytes on peripheral smear.

The patient was treated with polyvalent Anti-Snake Venom (ASV) serum injection from Haffkine Institute (Mumbai, India) which neutralises four most important venomous species found in India (Indian cobra, *Naja naja*; common krait, *Bungarus caeruleus*; Russell's viper, *Daboia russelii*; saw-scaled viper, *Echis carinatus*). In one hour after reconstitution of 10 vials of lyophilised ASV in 250 mL of isotonic saline, it was given intravenously. No adverse effects were detected with its administration. Two days later, patient developed anuria (urine output less than 100 mL/day) and facial puffiness. Repeat laboratory investigations revealed Hb 5.5 gm%, Platelet count 11000/mm^3 and TLC 10000/mm^3, serum creatinine 5.6 mg%, urea 144 mg%, sodium 140 mEq/L and potassium 5.8 mEq/L. Peripheral smear was suggestive of schistocytes (Black arrow) [Table/Fig-1]. Seum Lactatate Dehydrogenase- 750 IU, direct and indirect Coomb's test was negative.



[Table/Fig-1]: Black arrow showing peripheral smear (Leishman Stain 100x) was suggestive of fragmented RBC (Schistocytes).

In view of rapidly declining renal function and in view of hyperkalemia the patient was taken for haemodialysis. Blood culture results were negative for *E.coli.* Investigation findings together with hypertension, thrombocytopenia, microangiopathic haemolytic anaemia, kidney injury prompted the diagnosis of HUS. A Disintegrin and Metalloproteinase with Thrombospondin Motifs type 1, member 13 (ADAMTS13) level and genetic studies were not done, owing to the unavailability of resources. Patient was continued on with daily haemodialysis seven days later, patient gradually recovered, with an increase in platelet count, haemoglobin. However, she continued to

be oliguric for more than four weeks and the need for haemodialysis persisted. The patient was discharged with a prescription of twice/week haemodialysis. The patient did not revisit for future follow-ups.

DISCUSSION

Snake envenomation is a major and common cause of AKI in tropical countries like India. There are more than three million snake bites per year, and more than 1,50,000 deaths worldwide [1]. In rural India, snake envenomation is an occupational hazard, with most bites occurring in farms working barefoot or walking in the fields during the night. There are four families of poisonous snakes: Elapidae, Viperidae, Hydrophidae and Colubridae [1]. The most common clinical effects of elapid venom are neurotoxic, whereas those of vipers are vasculotoxic and Hydrophiinae or sea snakes are myotoxic. Viper bites are the most common in India and the incidence of AKI following Russell's viper and *E.carinatus* bites is 13-32% [2]. AKI is a common manifestation of snake envenomation and a significant cause of death and morbidity. Acute Tubular Necrosis (ATN) is the most common cause of AKI in this scenario with 75% of ATN-related cases [2] followed by Acute Interstitial Nephritis (AIN) in 5-15% of cases [3]. Intravascular coagulation is considered to be the cause of Acute Renal Failure (ARF) in this condition on the basis of ultrastructural findings [4], and because of the known coagulant properties of Russell's viper venom [5].

The TMA is rarely reported as a cause of AKI following snake envenomation. It has been linked to a triad of Microangiopathic Haemolytic Anaemia (MAHA), thrombocytopenia, and long-term renal failure following Venom-Induced Consumption Coagulopathy (VICC) resolution, or to an increased risk of acquired HUS-like condition [2]. The triad of Acute Renal Failure (ARF), thrombocytopenia and haemolytic anaemia with scattered erythrocytes (schistocytes) constitutes HUS [6]. In most cases, the lack of a full triad may be due to an incomplete or prolonged investigation. Intravascular coagulation would also result in the accumulation of platelet deficiency coagulopathy and fibrin strands in small blood vessels, which would split the erythrocytes and thus create the HUS triad [7].

Venom-Induced Consumption Coagulopathy (VICC), characterised by delayed clotting times, hypofibrinogenemia, and elevated D-dimer, is the most prevalent haemotoxin mediated coagulopathy generated by snake poisoning. After the poisons are neutralised, VICC dissolves at a rate compatible with the production of new clotting factors. The key complication is bleeding. VICC is distinct from the spread of Disseminated Intravascular Coagulation (DIC) [8]. VICC causes TMA in a limited percentage of snake bite victims (TMA). Long term outcomes and the optimal therapy for snakebite-related TMA remain unknown, as most reported cases, small case series, or other small retrospective observational studies are solitary instances, small case series, or other short retrospective observational studies [8]. HUS is characterised by the presence of microangiopathic haemolytic anaemia, thrombocytopenia, and AKI simultaneously [9].

Pathogenesis of AKI in snake envenomation includes hypotension, haemolysis, rhabdomyolysis, DIC, direct cytotoxic effect of the venom, sepsis, haemodynamic alterations, and cell damage triggered by the release of proinflammatory cytokines and vasoactive mediators [10]. Traditionally, coagulopathy in snake bites has been referred to as DIC. Recently, VICC has been identified because it better describes the clinical features and lack of other features of the DIC [11]. VICC is characterised by bleeding without evident fibrin deposition, microvascular thrombotic obstruction, or non renal end organ failure and is due to the action of snake toxin in the coagulation pathway, not to the tissue factor/factor VIIa pathway [11]. VICC is characterised by extended clotting periods due to activation of the coagulation cascade by thrombin like enzymes, prothrombin, and factor X activator in the venom. TMA is seen in a group of individuals who have been bitten by a snake and have either VICC or TMA [12]. Venom or its vascular endothelial toxins, which act as von Willebrand factor activators or vascular endothelial growth factor-like factors and cause TMA by causing endothelial damage, are the hypothesised mechanism [12].

In a 2007 study by Isbister GK et al., showed 13% of cases with brown snake envenomation were found to have features of TMA, indicating that TMA may have been missed in most of the previous studies [13,14]. This may be explained by the co-existence of VICC in most cases, which makes the diagnosis of TMA complicated, with clinicians wrongly attributing MAHA, thrombocytopenia, and renal damage to DIC [2]. In a 1999 study by Small G et al., the authors concluded that renal function cannot be definitely predicted and properly evaluated at one year after HUS. Renal function, on the other hand, was within normal ranges and remained steady in most children between one and five years after HUS. Longer term follow-up should generally be limited to individuals having proteinuria, hypertension, abnormal ultrasonography, and/or impaired Glomerular Filtration Rate (GFR) at one year, according to the research [15].

Plasma exchange can be considered in patients who are refractory to traditional ASV treatment. In addition to toxin removal, mediators of inflammatory and coagulopathic pathways produced by snake toxins may be removed, possibly saving the lives of severely sick patients [16]. Plasma exchange's therapeutic indications and efficacy in snake bite envenomation are unknown. While immune complexes and toxins were removed during plasma exchange, studies showed no difference in timing of renal recovery, anaemia, and platelet count between treatment with or without plasmapheresis [12].

CONCLUSION(S)

Snake bite is a significant cause of AKI in tropical countries. The risk of TMA should be considered in patients with snake bite with acute kidney damage, thrombocytopenia, microangiopathic haemolytic anaemia and normal coagulation profile. Early diagnosis and early dialysis and plasmapheresis in refractory cases can improve the renal outcome.

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