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CASE REPORT

Venom-induced consumption coagulopathy (VICC), thrombotic microangiopathy and rhabdomyolysis in Russell's viper bite

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Abstract

Background: Russell's viper is one of the most venomous snakes found in Bangladesh. Acute kidney injury (AKI) is a devastating complication of viper bite causing significant morbidity and mortality. We report a case of Russell's viper bite who presented with venom-induced consumption coagulopathy (VICC), thrombotic microangiopathy (TMA) and rhabdomyolysis. He was treated with antivenom and repeated hemodialysis and subsequently discharged.

Case presentation: A 60-year-old farmer presented with history of Russell's viper bite with local swelling without neurological involvement. His 20-minute whole blood clotting test was positive. After initial assessment, polyvalent antivenom was administered. Subsequently, he developed AKI, anasarca, high blood pressure (210/110mmHg), moderate anemia, edema (+++), bilateral crepitation at both lung fields. His blood report was suggestive of DIC, rhabdomyolysis and AKI. He was treated with blood transfusion and repeated haemodialysis. Renal biopsy revealed renal cortical necrosis with thrombotic microangiopathy. After 3 weeks of repeated hemodialysis, his condition improved and finally discharged.

Discussion: Russell's viper causes coagulopathy, nephrotoxicity, neurotoxicity, myotoxicity and cardiotoxicity. It causes VICC leading to occlusion of small and large vessels. AKI may result from hypovolemic shock, rhabdomyolysis and acute tubular necrosis that results secondary to VICC. Our patient had local swelling, coagulation abnormality, thrombocytopenia, high CPK, high LDH, schistocytes, high D-dimer, raised indirect bilirubin and raised serum creatinine confirmed the presence of VICC, TMA and rhabdomyolysis. The findings of microangiopathic hemolytic anemia, thrombocytopenia and cortical necrosis strongly suggest DIC as the culprit for the renal lesions in the patient. Although DIC with marked thrombocytopenia had a high mortality, our patient got antivenom and hemodialysis early for which he survived.

Conclusion: TMA, cortical necrosis and rhabdomyolysis causing AKI are some of the rare but lethal complications following Russell's viper bite. Prompt treatment with antivenom, haemodialysis and other supportive management is essential to save the life of the patient.

Keywords: Russell's viper, Venom-Induced Consumption Coagulopathy (VICC), Thrombotic Microangiopathy (TMA), Rhabdomyolysis, Acute Kidney Injury (AKI)

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INTRODUCTION

Snakebite is quite common in Bangladesh. More than 700000 bites and 6000 deaths happen yearly across the country which increases health burden [1]. Among the common snakes, Russell's viper usually bites the farmer creating significant occupational hazards throughout the country. Most patients present with predominant local features such as pain, swelling and blistering in the bitten area, rhabdomyolysis, intracranial vascular complications, intravascular coagulopathy, acute kidney injury and respiratory muscle paralysis. Thrombotic microangiopathy is a rare but recognized complication of Russell's viper envenomation. To our knowledge, no case of Russell's viper bite with VICC, thrombotic microangiopathy and rhabdomyolysis has been reported from Bangladesh. Here, we report a case of a middle-aged patient who presented with VICC, thrombotic microangiopathy and rhabdomyolysis due to Russell's viper bite.

CASE PRESENTATION

A 60-year-old previously healthy farmer hailing from Chandpur, Bangladesh was bitten on his hand accidentally

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while putting a snake into a case after rescuing it from a paddy field. Initially, there was a bite mark on his hand and he did not seek any medical advice. He went to a hospital after the affected hand began swelling. In the hospital, the snake was identified as Russell's viper (Figure 1). He complained of local pain and swelling of the left upper limb. He also complained of generalized bodyache. He had no focal neurological signs and he was conscious, cooperative and oriented to time, place, and person. Initially, he had no history of fever, vomiting, gum bleeding, hematuria or reduced urinary output. His 20-minute whole blood clotting test (WBCT) was positive. His pulse was 80 beats/min, blood pressure was 130/80 mm Hg, affected limb was swollen and tender. Other systemic examinations revealed no abnormality. After an initial assessment, 10 vials of polyvalent antivenom were administered. After 1st dose of polyvalent antivenom, he developed reduced urinary output and generalized swelling of the whole body. On examination, his blood pressure was rising (210/110mmHg), he was moderately anemic, edema (+++), bilateral crepitation at both lung fields and moderate ascites. His blood report was suggestive of disseminated intravascular coagulation, rhabdomyolysis along with acute kidney injury (Table 1). During this period, he was treated with blood transfusion and repeated haemodialysis. Then, renal biopsy was done to find out the cause of acute kidney injury. Renal biopsy revealed renal cortical necrosis with thrombotic microangiopathy (Figure 2). After 3 weeks of repeated hemodialysis, the patient improved and then discharged from the hospital.

Table 1. Investigation profile

Investigation	07/11/2023	14/11/2023	18/11/2023
Hb (g/dl)	11.3	6.4	9.4
TLC (/mm^3)	23,990	10,880	8,590
DLC (N/L%)	90/5	77/11	77/9
Platelet (/mm^3)	63,000	1,25,000	154000
Peripheral blood film	Schistocytes		
S. Creatinine	6.2mg/dl	6.29mg/dl	3.12mg/dl
S. Electrolyte ($Na^+/K^+/Cl^-/HCO_3$)	(130/4.2/103/24)	(132/3.5/95/23)	(135/4.1/103/24)
Urine R/M/E	Protein +++ RBC – Plenty	Protein + RBC – 8-12/HPF	
S. Bilirubin	3.2mg/dl		
Serum Bilirubin (Indirect)	2.6mg/dl		
D-dimer	>10mg/l		
aPTT	46 sec	26.7 sec	
PT	18 sec	14.7 sec	
Fibrinogen level	463mg/dl	354mg/dl	
Creatinine phosphokinase (CPK)	4322U/L		
S. Albumin	2.5g/dl		
USG of whole abdomen		Moderate ascites with bilateral pleural effusion	
S. Calcium	7.40gm/dl		
iPTH	45.8pg/ml		
Lactate dehydrogenase (LDH)	1034U/L		
Renal biopsy	Renal cortical necrosis withmicrovascular thrombi		

DISCUSSION

Russell's viper (family Viperidae, subfamily Viperinae, genus Daboia) is distributed erratically in 10 South Asian countries including Srilanka, India, Bangladesh, China and Taiwan. It is a medically important venomous snake and one of the leading causes of fatal snake bites in Pakistan, India, Bangladesh, Sri Lanka, Burma and Thailand [2,3]. It causes significant morbidity and mortality in agricultural field workers making it an important occupational hazard in this subcontinent [4]. 41 different venom proteins from 11 different protein families were identified from Russell's viper venom. Phospholipase A_2 (70%), snake venom serine proteinase and snake venom metalloproteinase are most important among them [2,5]. The venom proteomes are consistent with the enzymatic and toxic activities of the venom and correlate with the clinical manifestations of D. russelii envenomation which include local swelling haemorrhage, coagulopathy, renal failure, neuro-myotoxicity and intravascular hemolysis. Other clinical features include myonecrosis evident by severe pain and muscle tenderness with rhabdomyolysis and myoglobinuria, neurotoxicity, spontaneous hemorrhage and shock [6, 7]. Many of these complications are devastating and some of them are fatal. These complications depend on the severity of envenomation

Figure 1. The culprit Rusell's viper of our patient

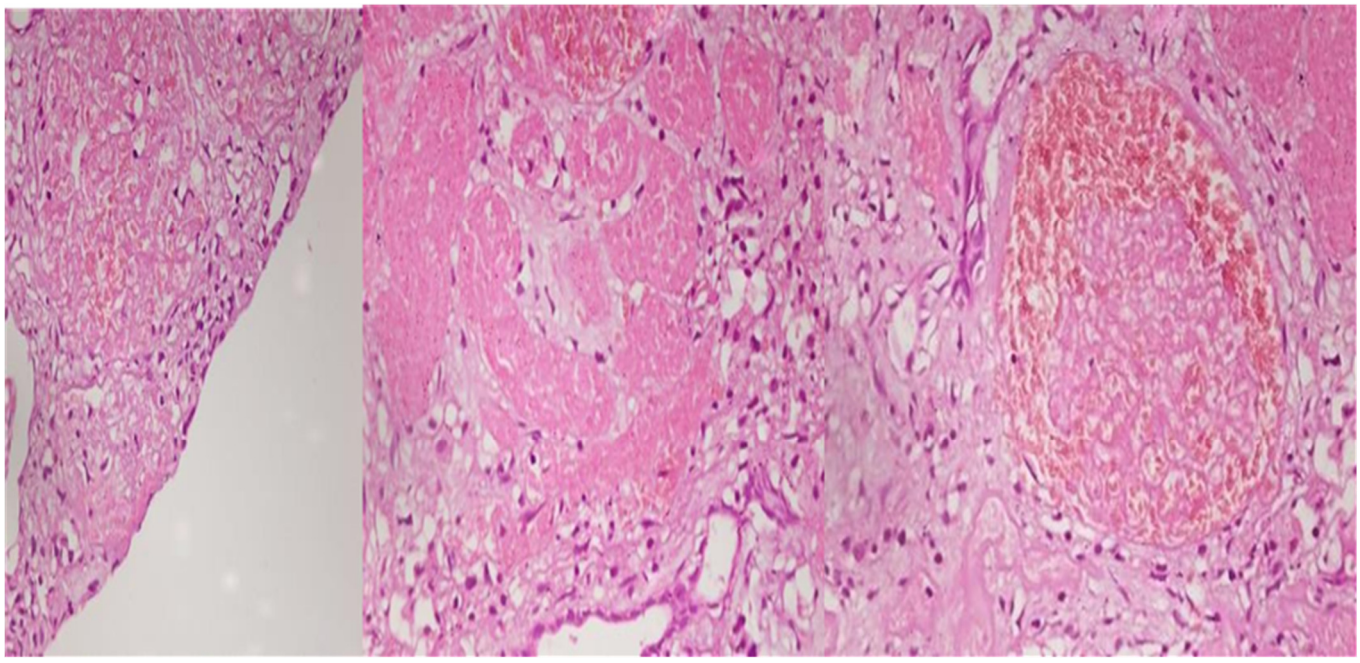

Figure 2. Renal biopsy showing renal cortical necrosis with microvascular thrombi

[8]. Clinical renal manifestations of Russell's viper include proteinuria, hematuria and renal failure. Renal pathologic changes include tubular necrosis, cortical necrosis, interstitial nephritis, glomerulonephritis, and vasculitis. Hemodynamic alterations caused by vasoactive mediators and cytokines and direct nephrotoxicity account significantly for the development of nephropathy. Hemorrhage, hypotension, disseminated intravascular coagulation, intravascular hemolysis, and rhabdomyolysis enhance renal ischemia leading to renal failure. Enzymatic activities of snake venoms account for direct nephrotoxicity. Immunologic mechanism plays a minor role [9,10]. Mortality risk is assessed by the VENOMS (Viper ENvenOming Mortality Score) model including 7 admission clinical parameters (these are recorded in the first 48 hours after bite): presence of overt bleeding manifestations, presence of capillary leak syndrome, haemoglobin <10 g/dL, bite to antivenom administration time > 6.5 h, systolic blood pressure < 100 mm Hg, urine output <20 mL/h in 24 h and female gender. The lowest possible VENOMS score of 0 predicted an in-hospital mortality risk of 0.06% while highest score of 12 predicted a mortality of 99.1% [11]. Other factors of mortality and morbidity are extensive agricultural practices, the abundance of venomous snake species, dense population and an overall lack of knowledge about primary treatment (first aid), nocturnal bites, severe leucocytosis on day 1, AKI, capillary leak syndrome and a need for more than 20 vials of ASV [9,12]. Acute kidney injury is an important cause of significant mortality and morbidity. AKI may result from both hemotoxin and nephrotoxin as direct nephrotoxic effect of snake venom, and fibrin thrombi in renal capillary [13-15]. Russell's viper causes VICC leading to occlusion of small and large vessels. VICC may also result from coagulation pathway activation due to snake toxin-like thrombin-like enzymes, prothrombin activators and factor X activators [16]. Acute tubular necrosis, acute interstitial nephritis, acute cortical necrosis (ACN), and thrombotic microangiopathy (TMA) are the common renal biopsy findings determining the cause of acute kidney injury. Vasculitis changes in vessels were rarely reported. Lesions such as ACN and TMA were associated with poor outcomes [17]. VICC is diagnosed by 20-minute whole blood clotting test (WBCT) in poor resource setting. Prothrombin time (PT) is also used for diagnosing VICC. The WBCT-15 had the best sensitivity of 47% for detecting VICC and 68% for complete VICC [18]. However a negative WBCT led to delayed antivenom administration [19]. Thrombotic microangiopathy (TMA) is a clinically important complication of snakebite associated with acute kidney injury. It presents with microangiopathic haemolytic anaemia and thrombocytopenia. AKI occurs in 94% of TMA patients. Majority of patients with AKI require dialysis, plasmapheresis is another treatment option. AKI improves in most cases [20,21]. Polyvalent antivenom is the primary therapy for Russell's viper bite [22]. The heterogenicity in the venom toxicity and neutralization potency of the antivenom is evident in individual data. Antivenom accelerated the recovery of VICC in patients with Russell's viper envenoming. Delay in antivenom administration is associated with increased mortality and morbidity [23, 24]. Management of patients with multiorgan failure is challenging especially if the presentation is late [25].

As our patient presented with swelling and had coagulation abnormality, thrombocytopenia, high CPK, high LDH, presence of schistocytes, high D-dimer, raised indirect bilirubin and raised serum creatinine confirmed the presence

of VICC, TMA and rhabdomyolysis. The findings of microangiopathic hemolytic anemia and thrombocytopenia in patientswith cortical necrosis strongly suggest DIC as the culprit for the renal lesions of snake-bite-induced cortical necrosis. According to the Journal of the Association of Physicians of India disseminated intravascular coagulation including marked thrombocytopenia had a mortality of 56%. It also showed that the shorter the interval between bite and renal shutdown, the poorer the prognosis [26]. Our patient got antivenom and hemodialysis early for which he survived.

CONCLUSION

Thrombotic microangiopathy, cortical necrosis and rhabdomyolysis causing acute kidney injury are some of the lethal complications following Russell's viper bite. Prompt treatment with antivenom, haemodialysis andother supportive management saved our patient. Although acute kidney injury is a common complication of Russell's viper bite, no case report has been published from Bangladesh yet.

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