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Ischemic cerebrovascular event amidst coagulopathy in snake venom envenomation: A case report

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ABSTRACT

This case report highlights the necessity to have in consideration about the ischemic complications post snake envenomation along with the traditional hemmorhagic events. We report a case of 28-year-old male who developed ischemic cerebral vascular accident post snake envenomation. The manifestations of snakebite may cause severe and sometimes fatal thrombotic or hemorrhagic sequelae. Some of these venom constituents and the mechanisms by which cerebral infarction have been discussed here. Physicians should also take into consideration that snake bite may cause both procoagulant and anticoagulant state. Complications can be prevented by prior identification of the snake bite and early administration of anti-snake venom.

Key words: Ischemic CerbroVascular Acident; Snakebite; Snake envenomation; Coagulopathy

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INTRODUCTION

Venomous snake bites contribute to significant morbidity and mortality worldwide. In India, snake bites and related deaths are not very uncommon. Predominantly, bites are more frequent among males, in the lower limb and during rainy season. Viper being the most common cause of bite, local envenomation is the frequent manifestation, followed by hemostatic and neurotoxic complications. In India, according to the estimate, 45,900 annual snake bite deaths occur.[1] India has more snakebites than any other country.[2] However, inadequate hospital-based reporting has resulted in estimates of total annual snakebite mortality ranging widely from about 1300–50,000. Snake envenomation is known to cause cerebral hemorrhage due to venom induced coagulopathy. However, cerebral ischemic events are a paradox and are rare with very few case reports in literature.

CASE REPORT

A 28-year-old male was brought to our hospital with alleged snake bite on the right lower limb (foot) 45 min before arrival. He had severe local pain, ecchymosis, and tense swelling around the bite site. Following that patient had a decrement in consciousness and developed respiratory distress. There was no history of bleeding from gums, epistaxis, hemoptysis, hematemesis, melena, and no focal neurological deficits. On arrival to the casualty, he was intubated with cuffed endotracheal tube in view of respiratory distress and low Glasgow coma scale (score-5).

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He was hemodynamically stable with a pulse rate of 100/min with regular rhythm. He was normotensive with blood pressure of 120/70 mmHg. However, he was tachypnoeic with a respiratory rate of 40/min. There was no cyanosis, pallor, clubbing, lymphadenopathy, and generalized edema and the jugular venous pressure was not elevated. His right leg was swollen up to the knee and had ecchymosis around the fang marks. Whole blood clotting time (20WBCT) was prolonged. Prothrombin time/activated partial thromboplatin time, International normalized ratio was not calculable. The other laboratory investigations are enlisted in Table 1. He was treated with polyvalent anti-snake venom (ASV) serum injection manufactured by the *Bharat Serums and Vaccines Limited* (Mumbai, India), which neutralizes four most important venomous species in India (Indian cobra, *Najanaja*; common krait, *Bungarus caeruleus*; Russell's viper, *Daboia russelli*; saw-scaled viper, and *Echis carinatus*). It was administered as an intravenous infusion over 1 h after reconstituting 10 vials of lyophilized ASV in 250 mL of isotonic saline. Ten morevials of ASV was repeated. No adverse reaction to its administration was observed. He developed hypotension in the following 6 h and required inotropes (started on injection norepinephrine). Compartment syndrome was relieved by fasciotomy and the coagulopathy was treated by fresh frozen plasma. The next day patient was conscious and could obey the commands. Neurological examination revealed right-sided hemiplegia with the right upper motor neuron lesion facial palsy. Pupils were bilaterally equal (3 mm) and normo-reactive to the light reflex and bilateral extensor plantar response was noted. Magnetic resonance imaging of brain showed acute infarct in left fronto-parietal and occipital lobe (Figure 1). Electrocardiogram, X-ray chest, and 2D-echocardiography were done to rule out cardio-embolic stroke. He had normal renal function tests on the day 1; however, his renal function tests were deranged for which hemodialysis was initiated through triple lumen curved hemodialysis catheter in the right internal jugular vein in view of non oliguric azotemia.

DISCUSSION

The two basic snake venoms are neurotoxic and hemotoxic. The venom which degrades neurotransmitters and depolarizes the axonal membrane, and inhibits the conduction of nerve impulses is neurotoxic venom. The venom which causes tissue destruction and also produces

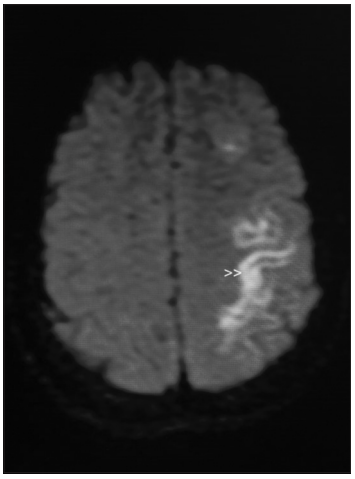

Figure 1: Magnetic resonance imaging showing acute infarct in the left fronto-parietal and occipital lobe

Table 1: Lab parameters of patient during the hospital stay

Lab parameters	Day of the hospital stay			
	Day 1	Day 2	Day 3	Day 4
Hemoglobin	15.6 g/dl		9.0 g/dl	
TLC	23,200 Cells/m^3		21,270 Cells/m^3	
Platelet	1.14		1.23	
Urea	16 mg/dl	37 mg/dl	67 mg/dl	
Creatinine	0.8 mg/dl	2.6 mg/dl	3.6 mg/dl	
Sodium	132 mmol/L	138 mmol/L	136 mmol/L	
Potassium	3.6 mmol/L	4.0 mmol/L	3.5 mmol/L	
Chloride	101 mmol/L	107 mmol/L	103 mmol/L	
T. bilirubin	2.2 mg/dl	3.1 mg/dl		
D. bilirubin	0.5 mg/dl	1.5 mg/dl		
AST	186 U/L	78 U/L		
ALT	98 U/L	53 U/L		
ALP	226 U/L	62 U/L		
GGT	84 U/L	56 U/L		
PT		Test 19.4, Control 10.6		
APTT		Test 30.6, Control 30		
INR	Not calculable	1.6	1.1	
LDH	529 IU/L			
Blood c/s				No growth

INR: International normalized ratio, PT: Partial thromboplatin, APTT: Activated partial thromboplatin time, TLC: Total leukocyte count, AST: Aspartate aminotransferase, ALT: Alanine transaminase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl tansferase, LDH: Lactate dehydrogenase

its effect is hemotoxic.[1] Hemotoxic snake venoms contain a wide variety of factors affecting the hemostatic mechanism which can be broadly classified as possessing anticoagulant, coagulant, and hemorrhagic mechanism.[3] Coagulant factors include activators of blood coagulation factors II (prothrombin), V and X; anticoagulants are protein C activators, inhibitors of prothrombin complex formation and fibrinogenases which are classified according to their specificity for the alpha-, beta-, and gamma-chains of fibrinogen. The thrombin-like enzymes are intermediate between true coagulants and true anticoagulants which bring about clotting *in vitro* but anticoagulation *in vivo*.

Ischemic stroke, following snake bite, is rare. Very few cases of ischemic stroke resulting from a snakebite have been reported. In an observational study of 309 cases of snake bite, Mosquera et al. reported cerebrovascular complications in eight patients (seven hemorrhagic strokes and one ischemic stroke).[4] Among the constituents in snake venom are a number of effects which are significant (either stimulatory or inhibitory) on hemostatic mechanisms, including the platelet function, coagulation, vascular integrity, and fibrinolysis.[5] The manifestations of snakebite may cause severe and sometimes fatal thrombotic or hemorrhagic sequelae. Some of these venom constituents have been isolated and their exact mechanisms are established. Apart from direct fibrinolysins, procoagulants predominate, most of them exert their effect late in the clotting cascade, activating factor X or prothrombin or directly converting fibrinogen to fibrin. The toxins which are well established pro-coagulant/platelet aggregating properties are cerastobin,[6] factor IVa,[7] cerastocytin,[8] and cerastotin.[9]

The mechanisms by which cerebral infarction occurs in snake envenomation can be multi-factorial and are as follows:

1. The procoagulant effect of the toxin leads to microthrombi, which causes cerebral infarction secondary to the occlusion of small and large vessels[10]
2. Toxic vasculitis post snake bite is caused by vascular spasm. Hemorrhagins are complement mediated toxic components which cause endothelial damage and increased vascular permeability. This toxic vasculitis results in thrombosis[10]
3. The venomous snake bite causes vomiting, sweating, bleeding tendencies superimposed decreased fluid intake leads to hypotension, and low flow state causing infarcts[10]
4. Hypovolemia and hypoperfusion secondary to hypotension cause hyperviscosity contribute to vessel occlusion[10]
5. Disseminated intravascular coagulation causes procoagulant phase by the consumption coagulopathy phase of DIC.[11]
6. Arrhythmias secondary to the cardiotoxic effects of the venom causes cardiac thromboembolism[10]

CONCLUSION

Here, we report a 28-year-old male who presented with a history of snake bite with systemic envenomation with coagulopathy. On evaluation for the right-sided hemiplegia, he was found to have acute infarct in the left fronto-parietal and occipital lobe. Thus, physicians should also take into consideration that snake bite may cause both procoagulant and anticoagulant state. Complications can be prevented by prior identification of the snake bite and early administration of ASV. Ischemic CVA can be managed by single or dual anti-platelet therapy warranted only if no bleeding manifestations and the anticoagulant state corrected. However, it is still not known whether similar ischemic events occur in other organs leading to their failure in snake envenomation.

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