

Thrombotic thrombocytopenic purpura in a patient with snake bite

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ABSTRACT

Snakebite envenomation is a common scenario in southern India. Among the various causes of acquired thrombotic thrombocytopenic purpura (TTP), snake bite envenomation is very rarely reported. We present a rare case of a 51-year-old man with TTP following snakebite envenomation. He developed features of TTP including impaired neurological state, renal dysfunction, low platelets, fever, microangiopathic hemolytic anemia on day 5 following snakebite. He received 7 cycles of plasma exchange and showed remarkable improvement. We are presenting this case to create awareness regarding TTP following snakebite as it has a very significant implication on treatment and mortality.

Keywords: Plasma exchange, Snake bite, Thrombotic thrombocytopenic purpura.

Snake bite envenomation is seen very commonly in India. As per WHO, India has an estimated 2.8 million snakebite cases cumulatively. Most of the patients are presented with either a neurotoxic or hematotoxic manifestations. Venom-induced consumptive coagulopathy (VICC) and disseminated intravascular coagulation (DIC) are common manifestations in the first 48 hours [1]. However, few patients go on to develop features suggestive of thrombotic thrombocytopenic purpura (TTP) which has to be aptly identified and will alter therapy [2]. We present a case report of a patient who presented with hematotoxic snake bite and went on to develop secondary TTP.

CASE HISTORY

A 51-year-old man with no known co-morbidities was presented with alleged history of snakebite on his left foot 2 days prior to admission to our hospital. Initially, he was taken to a nearby hospital where the whole blood clotting time was more than 20 minutes for which he received 30 vials of antisnake venom (ASV). He was shifted to our hospital where he was found to be breathless with a saturation of 88% on oxygen, blood pressure of 80/40mmHg, and deranged renal function. Fang marks associated with cellulitis was noted on the left foot.

He was intubated in view worsening respiratory distress, started on noradrenaline at 2.5mcg/kg/hr and renal replacement therapy. In view of coagulopathy, he received fresh frozen plasma (FFP) transfusion. Coagulopathy resolved in 24 hours of admission. He underwent debridement of the wound and was

started on broad injection piperacillin tazobactam and clindamycin for suspected cellulitis of left foot.

Laboratory workup showed low platelets (8000/mm³), activated prothrombin time of 31 seconds, International normalization ratio – 1.3, lactate dehydrogenase – 1851, and peripheral smear showed the presence of schistocytes. We also noted a decreasing trend in hemoglobin up to 6g/dl on day 4. He required multiple blood component transfusions, despite which a fall in platelets and hemoglobin with high LDH was noted. He needed dialysis in view of non-resolving acute kidney injury.

He was gradually weaned off inotropes and remained hemodynamically stable. However, his sensorium did not improve and was persistently restless and agitated. He underwent MRI brain and CSF analysis for the same which was normal. After multidisciplinary consult including a haematologist, a diagnosis of TTP was made and was started on plasma exchange on day 6. He received 7 cycles of plasma exchange. ADAMTS 13 level was done which was inconclusive. There was a gradual improvement in platelet count (>100,000/mm³ by 7th cycle) and his neurological status improved.

He underwent a tracheostomy in view of prolonged ventilation. He was gradually weaned off the ventilator. His sensorium improved and the response was appropriate. However, he continued to need dialysis. He was shifted to the ward, rehabilitation was continued, tracheostomy was decannulated, acute kidney injury (AKI) gradually resolved and was discharged home after a month of hospitalization. He was followed up in the hospital and is doing well.

DISCUSSION

Coagulopathy following snake bite (viper) has been described as DIC and venom-induced consumption coagulopathy (VICC). VICC is characterized by rapid onset coagulopathy within hours after the snake bite with elevated D-dimer levels, prolonged prothrombin time, and low fibrinogen levels which at times is associated with thrombocytopenia.^[1] This resolves within 24 to 48 hours. It is not associated with systemic micro-thrombi and end-organ failure [1].

Thrombotic microangiopathy (TMA) occurs in the subset of patients in snake bite envenomation with or without VICC. The proposed mechanism is venom or its vascular endothelial toxins may act as von Willebrand factor activators or vascular endothelial growth factor-type factors and initiate TMA by inducing endothelial damage. The role of ADAMTS-13, a von-Willebrand factor-cleaving protease in snake bite is unclear. Most of the reports of TMA, after snake bite, are from Sri Lanka and Australia. In many of the reports, there were features of DIC/VICC which later went on to develop TMA. Hence, it was not clear whether thrombocytopenia and microangiopathic haemolytic anemia (MAHA) occurred as a part of DIC [2]. Casamento et al presented two cases of TMA caused by envenomation of common tiger snake (*Notechisscutatus*). ADAMTS -13 levels were however normal in this report [3].

Syndromes suggestive of TTP-HUS spectrum has been reported in the literature with other venomous animal bites [4,5,6]. Ho *et al.*[7] report an interesting case of tiger snake. In this case, after an initial VICC, the patient had acute renal failure and a high LDH level with normal coagulation parameters. There was also MAHA that followed the resolution of VICC. The ADAMTS 13 levels, were normal. A case of TMA following Humped nose viper envenomation has been reported from Srilanka by Withana M et al [8]. ADAMTS-13 levels were not measured. Plasma exchange was done. T. Dineshkumar et al [9]. reported two cases of TMA from Tamil Nadu recently following viper envenomation. ADAMTS-13 levels were not measured in both the patients due to logistic reasons.

Most of the Indian patients who developed AKI are victims of Russell's viper and saw-scaled viper. Bites are characterized by local inflammation, blistering and tissue necrosis. Systemic envenoming may cause coagulopathy, acute kidney injury and death [2]. Thrombotic microangiopathy is an uncommon complication of snake envenomation.

Most cases of TTP are associated with a deficiency of the metalloproteinase ADAMTS 13, which is responsible for cleavage of unusually large von Willebrand factor multimers in plasma. Its deficiency results in accumulation of these multimers giving rise to platelet aggregation, microthrombi formation, and thrombotic microangiopathy [10]. Still, TTP can be observed in patients with normal ADAMTS 13 levels and proposed

hypotheses for pathogenesis in these circumstances include endothelial injury, increased platelet aggregation and increased levels of plasminogen-activator inhibitor type 1 (PAI-1). While primary or congenital cases of TTP are associated with a reduced level of ADAMTS 13, certain secondary causes of TTP may have normal levels of the enzyme [11,12].

The clinical indication and efficacy of plasma exchange in snake bite envenomation are unclear. American society for Apheresis has placed the role of plasmapheresis in envenomation as Grade 2C, Category 3 (weak recommendation, optimum apheresis therapy not established, the decision should be individualized) evidence [13,14]. In patients refractory to conventional therapy with anti-snake venom, plasma exchange can be considered. In addition to the removal of toxins, mediators of inflammatory and coagulopathic pathway invoked by snake toxins can be removed and may be lifesaving in severely ill patients.

We noted coagulopathy in our patient initially, which lasted for 48 hours and was associated with AKI suggesting VICC. There was a trend of low platelets, MAHA, rising LDH, worsening neurological state. We commenced him on plasma exchange and a gradual recovery was noted. However, the levels of ADAMTS -13 was normal in our patient as well. In our case, the patterns of onset of TTP is very similar to the above-reported cases with an initial VICC followed by TTP.

CONCLUSION

We have presented this case in view of creating awareness and to consider TTP as a differential following snake bite as it has a significant impact on treatment modality. Despite the role of plasma exchange remaining unclear in patients with normal ADAMTS - 13 levels, it seemed to have therapeutic benefit in our patient.

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