Case Report

Plasmapheresis in a Case of Acute Kidney Injury with Severe Hemolysis and Thrombocytopenia due to Hematotoxic (Russell’s viper) Snake Bite

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ABSTRACT. We present a case of a male patient after being bitten by a vasculotoxic snake (Russell’s viper) with severe hemolysis, thrombocytopenia, and acute kidney injury requiring hemodialysis. As attempt to administer anti-snake venom (ASV) failed because of development of anaphylactic reaction, a single session of plasmapheresis was done to stop hemolysis and fall in platelets, which was refractory to all other measures and proved to be a lifesaving procedure in this patient. The role of plasmapheresis in the management of snakebite victims is yet to be established, but can be beneficial in snake bite victims refractory to ASV or nonavailability of ASV or intolerant to ASV as in this case.

Introduction

Hematological abnormalities and acute kidney injury (AKI) following snake bite are common, but the exact pathogenesis for both is not well established. The most effective way to manage coagulopathy and AKI is early and adequate administration of anti-snake venom (ASV).¹ ASV carries risks of life-threatening anaphylactic reactions and should therefore be used with caution and preparation for any such reaction. Plasmapheresis is not a recommended therapy in the management of patients with snake bite envenomation as the efficacy of plasmapheresis is unclear.² Here, we present the case of a patient with AKI and severe coagulo-pathy after being bitten by a vasculotoxic snake (Russell’s viper) where the patient was intolerant to ASV and plasmapheresis was very helpful.

Case Report

Informed consent was obtained from the patient before presenting the report.

A 44-year-old male, with no relevant past medical history, presented to our hospital with AKI after being bitten by a snake (Russell’s viper) on his right lower limb two days back while he was going to defecate in the field. He was immediately taken to a practitioner of Ayurveda Indian medicine where he did not receive any ASV but was being managed conservatively with traditional medicines (unknown nature) for pain and swelling at the bite site.
When the patient experienced decreased urine output and uremic symptoms, he was referred to our hospital.

On arrival to our emergency room, the patient had cellulitis on the bite site with no bleeding from any site and no lateralizing neurological signs or symptoms. Blood pressure was 160/100 mm Hg and pulse rate was 110/min. Ultrasound revealed normal size kidneys with increased echogenicity and maintained cortico-medullary differentiation. The laboratory investigations are provided in Table 1.

A provisional diagnosis of AKI (hemolytic uremic syndrome) was made. ASV was not administered in view of normal 20-min whole blood clotting test (WBCT20) and no apparent bleeding. The patient was taken for hemodialysis (HD) along with platelet transfusion.

In the next 24 h, repeat laboratory tests were suggestive of ongoing hemolysis, with hemoglobin falling to <7 g/dL and platelets remaining below 10,000 despite multiple transfusions. Repeated investigations of prothrombin time-international normalized ratio (PT-INR), activated partial thromboplastin time, WBCT20 were always within normal limits. Patient continued to be anuric, dialysis dependent but hemodynamically stable. In view of ongoing hemolysis, methylprednisolone was given and when there was no effect ASV infusion was started.

Soon after starting ASV infusion, patient developed intense itching all over the body. Infusion was immediately stopped and injections promethazine and hydrocortisone were given. Plasmapheresis for AKI due to hematotoxic (Russell’s viper) snake bite

| Investigations                      | Results          | Normal values          |
|------------------------------------|------------------|------------------------|
| Hemoglobin                         | 11.1 g/dL        | 14–17 g/dL             |
| Total leukocyte count              | 30,600/mm³       | 4,000–11,000/mm³      |
| Platelet count                     | 10,000/mm³       | 150,000–350,000/mm³   |
| Creatinine/urea                    | 8.19/188 mg/dL   | 0.7–1.3 /13–43 mg/dL  |
| Na/K                               | 128/5.8 mmol/L   | 135–145/3.5–5.1 mmol/L|
| Total bilirubin/direct bilirubin   | 2.23/0.6 mg/dL   | 0.3–1.2 /0–0.3 mg/dL  |
| SGOT/PT                            | 590/229 IU/L     | 0–35 IU/L              |
| WBCT20                             | 8 min            | >20 minutes            |
| PT-INR                             | 1.03 %           | <1.5%                  |
| aPTT                               | 30.4 s           | 24–33 sec              |
| FDP                                | >20 µg/mL        | <10 mcg/mL             |
| Fibrinogen                         | 296 mg/dL        | 150–350 mg/dL          |
| Haptoglobin                        | 8 mg/dL          | 50–150 mg/dL           |
| LDH                                | 3806 U/L         | 60–100 U/L             |
| PBF                                | Fragmented RBCs seen |
| CPK                                | 4505 U/L         |                        |
| ANA/ANCA/HBsAg/anti-HCV/HIV        | Negative         |                        |
| Calcium/phosphorus                 | 9.6/4.5 mg/dL    | 9–10.5 /3–4.5 mg/dL   |
| Uric acid                          | 4.8 mg/dL        | 2.5–6 mg/dL            |
| D-dimer                            | >20 µg/mL        | less than 0.5 µg/mL    |
| Procalcitonin                      | 10.9 ng/mL       | less than 0.5 ng/mL    |
| Direct Coomb’s test                | Positive         |                        |
| Chest X-ray and ECG                | Normal           |                        |
| Urine S/M                          | Not done (anuria)|                        |

Na: Sodium, K: Potassium, SGOT: Serum glutamic oxaloacetic transaminase, PT: Prothrombin time, WBCT: Whole blood clotting test, INR: International normalized ratio, aPTT: Activated partial thromboplastin time, FDP: Fibrin degradation product, LDH: Lactate dehydrogenase, PBF: Peripheral blood film, CPK: Creatine phosphokinase, ANA: Antinuclear antibody, ANCA: Antineutrophil cytoplasmic antibody, HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus, ECG: Electrocardiogram, RBC: Red blood cell.
Snake bite is a common and frequently devastating environmental and occupational hazard, especially in rural areas of developing countries in tropical region. Kidneys have high vascularity, so are potentially susceptible to venom toxicity. In snake envenomation, the pathogenesis of AKI and renal pathological changes are various, but acute tubular necrosis (ATN) occurs for majority of AKI following snake bite, and most of these cases are self-limiting and resolve completely within one to eight weeks. Renal biopsy could not be done in our case, but the clinical course was typical of a case of ATN, recovering his renal functions within three weeks of injury.

There is a wide variation in hematological abnormalities following a snake bite. Twenty-minutes whole-blood clotting time is the most reliable test of coagulation and if incoagulable blood is found, ASV should be administered. This case presented to our hospital two days after the snake bite, and repeated samples of WBCT20 were within normal limits. Hence, ASV was not administered on the day of admission. However, the ongoing hemolysis and continuous fall in platelets, prompted us to administer ASV, which could not be done because of the development of anaphylactic reaction.

The most common coagulopathy associated with snake envenomation is venom-induced consumption coagulopathy (VICC) which results from the activation of coagulation pathway by snake toxins. It causes elevated D-Dimer, low fibrinogen, and prolonged prothrombin time, all of which are features that overlap with disseminated intravascular coagulation (DIC). In this case, though D-dimer values were high, repeated samples of PT-INR and fibrinogen were within normal limits, thereby making a diagnosis of VICC or DIC unlikely.

Thrombotic microangiopathy (TMA) occurs in the subset of patients in snake bite envenomation with or without VICC, although the exact mechanism remains largely unknown. While the coagulopathy in VICC resolves rapidly, the triad of TMA (AKI, thrombocytopenia, and microangiopathic hemolytic anemia) persists for longer time period. Most of the reports of TMA after snake envenomation are...
from Sri Lanka and Australia; few cases have been reported from India.\(^3\) As the triad of TMA was persisting in our case, the underlying TMA recovering dramatically after a single session of plasmapheresis seems unlikely as most of these patients require multiple sessions of plasmapheresis before registering any clinical benefits.\(^6\)

Timely administration of antivenom is the only specific treatment to reverse the coagulopathy associated with snake bite.\(^3\) Limited availability and risks of sometimes life-threatening side effects such as anaphylactic reactions, as in our case, have prompted research into alternative antivenom therapies, none of which have shown much promise till date.\(^3\) While supportive care with RBCs, FFP, and platelet transfusions along with ASV forms the basis of treating these patients, we used high-dose corticosteroids in an attempt to modify suspected complement-mediated hemolysis with no beneficial effects. While corticosteroids are widely used in other hemolytic conditions, there is no medical literature regarding their efficacy in snake envenomation.\(^7\)

The clinical indications and efficacy of plasmapheresis in the management of snake bite victims are unclear and therefore is not a recommended therapy. However, successful applications of plasmapheresis in snake bite victims including patients with coagulopathies have been previously noted.\(^2,6\)

While the causation cannot be demonstrated from this case report, we did observe an association between initiation of plasmapheresis and reversal of downhill course of clinical condition. Theoretically, plasmapheresis may have removed the venom,\(^7\) resulting in clinical improvement, but plasmapheresis was done four days after the bite, making this hypothesis unlikely in our case. Venom that diffuses out of the blood compartment is not effectively removed; however, redistribution and elimination of venom toxins from extra-vascular space and target tissues may occur with plasmapheresis.\(^6\)

The beneficial effects of plasmapheresis in this patient may be due to removal of complement components (mediators of inflammatory and coagulation pathways) activated by snake venom as well as removal of immunoglobulin G. This hypothesis is further supported by positive direct Coomb’s test in our case, leading to rapid reversal of ongoing hemolysis and fall in platelets. ATN took its natural course of three weeks to recover when the patient started making urine and became dialysis independent.

Whether the use of traditional Indian medicines in this patient were causing confusing signs and symptoms or there are some unknown mechanisms through which plasmapheresis is beneficial cannot be contemplated from this case and requires further investigation.

### Conclusion

In snake envenomation, for patients with AKI and coagulopathy, refractory to conventional therapy with ASV or intolerant to ASV or nonavailability of ASV, plasmapheresis can be considered and it may be a lifesaving measure in severely ill patients as in this case. The American Society of Apheresis has placed the role of plasmapheresis in snake envenomation as Category 3 (weak recommendation, optimum apheresis therapy not established, decision should be individualized) evidence.\(^3\)

### Conflicts of interest:
None declared.

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