A CASE OF VIPER SNAKE BITE PRESENTING WITH GANGRENE AND SEPSIS ASSOCIATED MULTIORGAN FAILURE, SUCCESSFULLY TREATED WITH CYTOSORB® AS AN ADJUNCT THERAPY- A CLINICAL EXPERIENCE

Rajib Paul1, Brajesh Kumar Jha2, Vikram Kumar Shetty3

1Senior Consultant and Intensivist, Department of Internal Medicine and Critical Care Apollo Hospital, Jubilee Hills, Hyderabad.
2Medical Affairs, SBU, Biocon Ltd., Bangalore.
3Medical Affairs, SBU, Biocon Ltd., Bangalore.

HOW TO CITE THIS ARTICLE: Paul R, Jha BK, Shetty VK. A case of viper snake bite presenting with gangrene and sepsis associated multiorgan failure, successfully treated with Cytosorb® as an adjunct therapy- a clinical experience. J. Evid. Based Med. Healthc. 2018; 5(6), 559-561. DOI: 10.18410/jebmh/2018/114

PRESENTATION OF CASE
Viper snake bites are known to cause local complications like necrosis and cellulitis and systemic complications such as coagulopathy, acute renal failure (ARF), and haemolysis. We report a case of 32-year young male patient who was bitten by a viper. He developed cellulitis, sepsis, acute renal failure, and disseminated intravascular coagulation (DIC). Patient also developed acute respiratory distress syndrome (ARDS) probably due to the direct toxic effect of venom on pulmonary vascular endothelium. He was treated with standard care of treatment along with a novel extracorporeal cytokine adsorption device Cytosorb® as an adjunct therapy. After Cytosorb® treatment, all his renal, haematological and respiratory parameters returned to normal. The post-Cytosorb® APACHE II and SOFA score was reduced to 11 and 8 from a baseline value of 29 and 15 respectively.

A 32-year-old male was admitted with the history of snake bite over the dorsal surface of right lower limb. The snake in this case was identified as a viper. He was immediately treated with polyvalent anti snake venom (ASV) elsewhere in local hospital.

After few days, he was admitted to our hospital having developed extensive cellulitis leading to necrotizing fascitis of right lower limb. There was wet gangrene of the right lower limb up to the knee level. A clinical diagnosis of limb gangrene with septicaemia was entertained. Lower limb amputation was performed. He was optimized (fluid resuscitation, blood transfusion, tetanus toxoid administration, ceftriaxone and combination of antibiotics) for an emergency in surgery unit. Following amputation, patient was drowsy, hypotentive and in septic shock condition. Patient was shifted to ICU. The sepsis severity score i.e. APACHE II and SOFA on ICU admission were 29 and 15 respectively.

CLINICAL DIAGNOSIS AND PATHOLOGICAL DISCUSSION
It is evident that the differences between the venom constituents of various snake species are the results of a diet/prey directed evolution.1 Venom is often watery. Enzymatic proteins of class proteases, collagenase, and arginine ester hydrolase have been identified in viper venom. Function wise details of several enzymes present in venom are namely, hyaluronidase, responsible for rapid dissemination of venom through subcutaneous tissues by disrupting mucopolysaccharides; phospholipase A2, plays a major role in haemolysis and promotes muscle/tissue necrosis; and thrombogenic enzymes, promote the formation fibrin clot, which, in turn, activates plasmin and results in a coagulopathy and hemorrhagic manifestations. Enzyme concentrations vary among species, thereby exhibiting non-uniform envenomations.

The viper venom has thrombin-like actions which cause local vasculopathy resulting into swelling, blisters and necrosis. The chance of tissue necrosis with viper venom is 2-3%.2 This localized injury is a harbour for bacterial growth, and further, it can cause septicemia also. Studies support the high chance of necrosis at the site of viper bite. Disseminated intravascular coagulation may be due to spontaneous activation of factor V and factor X by pro-coagulants present in the venom. This results in the assembly of a fibrin leading to bleeding manifestations. Direct vascular endothelial damage caused by the direct effect of the venom may also contribute to hypovolemic manifestations. Our patient had local and multiple systemic manifestations which were early as well as late.

Local pain, swelling, bleeding from bite site, necrosis, and cellulitis are early manifestation.3 The systemic bleeding manifestations include DIC primarily due to direct endothelial damage by venom and secondly, due to procoagulant activity and prolonged defibrination.4 This can happen within minutes or after several hours or days. In such patients ARF can develop early as well as late. Occlusion of renal vessels by microthrombi, ischemia, and shock are the attributing factors for ARF.5 6 Also, haemoglobinuria and myoglobinuria cause nephrotoxicity, leading to ARF. Hypovolemia caused by loss of plasma and blood lead to late shock.7 The possible cytokine storm leading to endothelial cell damage can be a major contributing factor for sepsis associated multiorgan failure (MOF) in the cases of snake envenomation.
Host immune responses to snake venom which results into elevated cytokines release may contribute to the severity of these symptoms, however, have not been well characterized in humans. In acute management of snake bite we almost always tend to overlook possible sepsis even after identifying the snake. Extracorporeal cytokine adsorption device (ECAD) Cytosorb® (Cytosorberts Corporation, USA) targets cytokines, helps modulate immune response and prevent multiorgan failure. Cytosorb® is considered to be a successful adjunctive therapy in patients with elevated cytokine levels in severe sepsis, septic shock and to also reduce bilirubin along with various toxic metabolites.\(^8\)

In the present case, patient developed cellulitis, sepsis, ARF, and DIC. Patient also developed ARDS. In view of the multiorgan failure, patient was treated with ECAD (Cytosorb®) along with standard care of treatment as per the international sepsis guideline.

**DISCUSSION OF MANAGEMENT**

On ICU admission, patients’ hemoglobin was 9.7 g/dl, total leukocyte count was 32,000/mm\(^3\) with 72% neutrophils, and platelet count was 52,000/mm\(^3\). Coagulation profile revealed bleeding time of 8 min. 15 sec., clotting time of 12 min., prothrombin time of 55 sec., and the activated partial thromboplastin time of 60 sec. On examination, he was found to be febrile, lethargic, tachypneic and maintaining saturation 99% at room air with Pulse Rate (PR)-116/min.

On the first of ICU admission, in view of thrombocytopenia patient was transfused with four units of fresh frozen plasma and four units of platelet concentrate. Input and output charting along with central venous pressure monitoring was carried out along with fluid resuscitation. Multiple episodes of severe hypotension and bradycardia were treated with adrenaline, noradrenaline, dopamine and increased dose of inotropic agents. On second day, in spite of this treatment, he continued to have breathlessness, decreased urine output, evidence of haemolysis, deranged blood urea and creatinine levels. His respiratory rate was 45-50 per minute and ABG showed pH 7.45, PCO2 50 mm Hg, PO2 35.2 mm Hg, HCO3 27 mmol/l, SO2 65.1%. Chest radiograph showed bilateral fluffy opacities. (Figure). On the basis of above findings, a diagnosis of acute ARDS was made and he was immediately intubated and put on volume control mode of ventilator with high PEEP, low tidal volume (355 ml), and high FiO2 (100%).

On the 3rd day the decision to commence haemadsorption with Cytosorb® was taken. Blood flow was maintained at 120 ml/min without anticoagulant. The adsorber was placed in a post dialyzer position. The procedure was maintained for 18 hours for each device.

Considering the lack of evidence in snake envenomation, only two ECAD was used.

After two subsequent Cytosorb® on 24-hour interval, renal, hemodynamic and respiratory parameters improved remarkably and attained normalized values over 5 days. His ventilator requirement of PEEP and FiO2 was significantly reduced and gradually weaned off the ventilator after Cytosorb® therapy. Similarly, significant improvements in the platelet counts were also achieved (Table). Chest radiograph also improved significantly (Figure). After Cytosorb® therapy, APACHE II and SOFA score was reduced to 11 and 8 from a baseline value of 29 and 15 respectively. Patient was discharged from ICU in afebrile condition.

**FINAL DIAGNOSIS**

In the present case report, despite the standard treatment of our intubated patient with thrombocytopenia, acute renal failure and ARDS, haemadsorption using Cytosorb® was deemed to be successful. Needless to say, Cytosorb® act as an immunomodulator in controlling the cytokine storm.

As far as the treatment outcome of haemadsorption using Cytosorb® in viper snake bite patients is concerned, to the best of our knowledge, this case is the first report on the application of Cytosorb® in a snake bite case with sepsis and multiple organ failure; treated successfully along with standard care of treatment. However, since literature regarding haemadsorption in the snake bite cases is limited, larger prospective studies are required to evaluate the exact advantage and possible adverse effects.

Cytosorb® along with standard care can be a safe and advantageous extracorporeal therapy option to treat snake bite patients with multi organ failure to help them recover.

---

**Figure 1. Improvement in Bilateral Lung Infiltrates after 2-Cytosorb® device**

---

J. Evid. Based Med. Healthc., pISSN- 2349-2562, eISSN- 2349-2570/ Vol. 5/Issue 6/Feb. 05, 2018
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>Post-Cytosorb® (1st Device)</th>
<th>Post-Cytosorb® (2nd Device)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (gm/dl)</td>
<td>9.7</td>
<td>11.7</td>
<td>12.9</td>
</tr>
<tr>
<td>WBC count ( mm$^3$)</td>
<td>32,000</td>
<td>23,800</td>
<td>9,700</td>
</tr>
<tr>
<td>Platelet count ( /L)</td>
<td>52,000</td>
<td>82,000</td>
<td>120,000</td>
</tr>
<tr>
<td>D-Dimer (ng/ml)</td>
<td>1500</td>
<td>795</td>
<td>495</td>
</tr>
<tr>
<td>Urine output (ml/day)</td>
<td>150</td>
<td>250</td>
<td>450</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>195</td>
<td>46</td>
<td>29</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>9.86</td>
<td>3.26</td>
<td>1.21</td>
</tr>
<tr>
<td>Lactic acid (mg/dl)</td>
<td>4.3</td>
<td>1.6</td>
<td>0.9</td>
</tr>
<tr>
<td>PCT (ng/dl)</td>
<td>1.8</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Activated partial thromboplastin time (second)</td>
<td>60</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Arterial blood gas pH</td>
<td>7.45</td>
<td>7.40</td>
<td>7.35</td>
</tr>
<tr>
<td>Apache II</td>
<td>29</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>Sofia</td>
<td>15</td>
<td>11</td>
<td>8</td>
</tr>
</tbody>
</table>

**Table 1. Laboratory Parameters before and after Cytosorb®® therapy**

**REFERENCES**


