

# Capillary leak syndrome due to Russell's viper envenomation—A doomy presage for treating clinician

Hariharan A S, Shivkumar Gopalakrishnan, Bobby Abraham

Department of General Medicine, Government Villupuram Medical College and Hospital, Villupuram, Tamil Nadu, India

### ABSTRACT

Russell's viper envenomation is a major challenge to physicians providing intensive care due to diverse presentations and dismal outcomes. The venom can cause idiopathic systemic capillary leak syndrome manifesting with bilateral parotid swelling, hemoconcentration, and refractory shock. Physicians' awareness about this presentation is lacking. Delayed recognition of this syndrome leads to fatalities despite providing the best possible care. We hereby report a fatal case of Daboia russelii bite presenting as capillary leak syndrome. The aim is to create awareness among tropical physicians who are primary caregivers to these victims.

**Keywords:** Capillary leak syndrome, parotid swelling, Russell's viper envenomation

### Introduction

Globally, as many as 5.4 million people suffer from snakebite each year, 70% of which occurs in the Asian subcontinent with India being its snakebite capital.<sup>[1]</sup> The mortality, however, is underreported and, rightly so, because snakebite figures in the list of "Neglected Tropical Diseases" as per the World Health Organization (WHO) consensus statement.<sup>[1,2]</sup>

Russell's viper species is distributed widely in India and is arguably the most common cause for systemic envenomation. Nevertheless, clinical manifestations as well as venom composition of the snake are not uniform and display considerable biogeographic variation even within the country.<sup>[3]</sup> Although hemotoxicity and local tissue damage are the protean presentations of snake venom, there are the lesser recognized and more sinister manifestations that portend bad outcomes.

Physicians' awareness about such phenomena is crucial, lest the patient community suffers. We thereby aimed to put on record a unique clinical manifestation of Russell's viper envenomation that fatally struck the victim.

### Case Report

On March 31, 2021, a 43-year-old farmer was rushed to the emergency room (ER) at 12.30 hours for alleged history of snakebite over his left foot at 10.15 hours. The snake was later identified as Russell's viper, upon visual inspection. Critical assessment revealed patient to be in stupor (Glasgow Coma Scale [GCS] E2 M4 V1) and respiratory distress with SpO<sub>2</sub> of 81%. Examination showed pulse rate at 104/min and blood pressure at 100/82 mmHg with swelling and blood ooze from the site of the bite. Immediate respiratory support was initiated with invasive ventilation using volume-cycled assisted/controlled ventilation mode. Whole blood clotting test (WBCT) at 12.40 hours was positive (incoagulable). Shortly after hemodynamic stabilization, 100 ml of polyvalent equine antsnake venom (ASV; manufactured by Biological E. Limited, Hyderabad/Lyophilized ASV of batch A1603020/March/2020) was infused along with intravenous fluid support

**Address for correspondence:** Dr. Hariharan A S, Department of General Medicine, Government Villupuram Medical College and Hospital, Villupuram - 605602, Tamil Nadu, India. E-mail: hariharan.smia@gmail.com

Received: 08-12-2021  
Accepted: 04-02-2022

Revised: 01-02-2022  
Published: 14-10-2022

#### Access this article online

##### Quick Response Code:



Website:  
www.jfmpc.com

DOI:  
10.4103/jfmpc.jfmpc\_2385\_21

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Hariharan AS, Gopalakrishnan S, Abraham B. Capillary leak syndrome due to Russell's viper envenomation—A doomy presage for treating clinician. J Family Med Prim Care 2022;11:5670-2.

and injection Cefotaxime 1 gram bd. The patient was sedated with injection midazolam 3 mg iv stat dose; neuromuscular paralysis was maintained with injection pancuronium 2 mg IV every hour.

Blood investigations on day 1 revealed predominantly polymorph-rich leukocytosis (total count 46,800/ $\mu$ L, hematocrit 42.7%, and platelet count 53,000/ $\mu$ L). Liver function tests and serum electrolytes were within normal limits. Blood urea was 35 mg% and creatinine 1.3 mg%. WBCT was incoagulable at 12 hours after admission, so a further 100 ml of ASV was infused. Repeat WBCT at 24 hours was incoagulable as well, and another 100 ml of ASV was administered. At the end of day 1, a total of 30 vials of ASV had been administered. The urine output was 1,100 ml since admission.

On day 2, patient's hemodynamic parameters were under physiologic limits, but renal function tests showed elevation of blood urea (57 mg%) and creatinine (1.7 mg%). His urine output recorded over the next 6 hours showed a decline (130 ml). Patient's hematocrit rose to 44.8%, platelet count was 84000/ $\mu$ l, and the total count was still in polymorphic leukocytosis with a downward trend (total count 30,600/ $\mu$ L). Urinalysis revealed positivity for sugar and albumin. Clinically, patient's mentation improved (GCS 9/15, E3M5V1), and swelling at the bite site increased to reach the knee and painless parotid swelling developed first over left parotid and then right parotid [Figure 1]. In addition, the patient developed bilateral conjunctival edema and petechiae all over the body [Figure 2].

The ventilator settings were optimized to Synchronized Intermittent Mandatory Ventilation (SIMV) mode with a tidal volume of 8 ml/kg ideal body weight. Management focused on fluid replenishment to augment urine output and supportive respiratory and pain care.

On day 3, patient developed profound hypotension BP 80/60 mmHg and tachycardia 132/mt. His mentation

worsened (GCS 7/15, E2M4V1), and urine output further decreased (80 ml over 12 hours). Renal replacement therapy was planned but temporarily delayed due to hemodynamic instability. Despite inotropic support, patient's BP never improved and GCS further dropped to 3/15. Approximately 68 hours after bite patient suffered cardiac arrest and could not be revived.

### Ethics approval

Institutional Ethics Committee approval was obtained for publication of this work and the written informed consent obtained from the patient's spouse/guardian.

### Discussion

Idiopathic systemic capillary leak syndrome (ISCLS) is a rare and devastating phenomenon first reported and described by Clarkson in the late 1990s.<sup>[4]</sup> There are many etiologies among which viral hemorrhagic fever (Dengue) and Russell's viper envenomation are dominant causes in the tropics. Whereas incidences of mortality due to dengue have largely been curtailed, mortality caused by ISCLS of *Daboia Russelli* envenomation continues unabated and remains a major challenge.<sup>[1]</sup> There are multiple reasons for the dismal outcome of this condition. First, majority of snakebite victims are managed at the primary- and secondary-care-level hospitals where physicians' awareness of this critical illness is inadequate. Second, intensive monitoring- and management-centered infrastructure is deficient at these hospitals. Finally, the loss of valuable time in patient transfer compounds the scenario where patients are wheeled in late into the disease when few if any interventions would help.

The physiopathogenic cascade of ISCLS is initiated by vascular endothelial cell damage caused by Russell's viper venom component, namely, Snake Venom MetalloProteinase (SVMP).<sup>[5]</sup> Down the road, plasma and protein leak into interstitium thereby depleting the intravascular volume and creating dangerous hypoperfusion of vital organs.<sup>[6]</sup> The major manifestations of this syndrome are profound hypotension, hypoalbuminemia,



**Figure 1:** Bilateral parotid swelling Left > Right; 24 hours after snake envenomation



**Figure 2:** Petechiae over left arm and chest

hemoconcentration, parotid swelling, periorbital swelling, and conjunctival chemosis.<sup>[1,6]</sup> Other unusual presentations include pleural effusion, ascites, thrombocytopenia, and encephalopathy.<sup>[1]</sup> The mechanism behind parotid enlargement is supposedly due to increased capillary permeability and vascular leak.<sup>[1,5,6]</sup> It is presumed that the syndrome is more common in males, though unequivocal proof is lacking.<sup>[1]</sup>

The onset of parotid swelling and refractory shock in a patient following Russell's viper envenomation should alert the treating clinician to suspect capillary leak syndrome as it carries up to 100% mortality. Once ISCLS is established, defibrination, hemorrhage, shock and acute kidney injury develop with frightening rapidity.<sup>[1,7,8]</sup> Crucial warning indicators of ISCLS include hemoconcentration, leukocytosis, and pleural effusion, which should be anticipated and actively screened for in Russell's viper envenomation. Intensive care personnel working in the field need to be cognizant of these signs that, if disregarded, could have devastating consequences. Monitoring and critical care should accordingly be scaled up to prevent death in such situations.

The crux of management lies in early identification and meticulous hemodynamic monitoring and support.

Therapy is best guided by central venous pressure—monitored infusion of intravenous fluids to maintain vital organ perfusion.<sup>[9]</sup> An alternative in resource-poor settings could be urine output—dependent fluid replenishment strategy. The role of intravenous volume expanders has been controversial and cannot be universally recommended as yet.<sup>[9]</sup> Inotrope support finds a less prominent role that should be employed in cases of refractory shock despite adequate fluid resuscitation or contraindications for the same. The vasopressor of choice is norepinephrine.<sup>[9]</sup>

Our patient was brought to the hospital at an appropriate time and managed as per national/WHO protocol. Russell's viper population of Southern India and Sri Lanka is notoriously infamous for causing neuromuscular toxicity as well, which explains the need for mechanical respiratory support in our patient.<sup>[3]</sup> Notwithstanding our best efforts, his disease course was tumultuous and downhill with a transient improvement on day 2. With the onset of parotid swelling and clinical shock, there was a disastrous decline in vital organ function marked by falling urine output and worsening encephalopathy. The patient could probably have benefitted from advanced shock management strategies like intra-aortic balloon pump (IABP), which uses counter pulsation or Extracorporeal Membrane Oxygenation (ECMO), but, it was unfortunately beyond the scope of our institute.

## Conclusion

Bilateral parotid swelling, conjunctival edema, and hypotension are components of ISCLS due to Russell's viper bite. Physicians' awareness of this condition needs to be enhanced by training sessions and infotech aids. In the rural tropics of India, the syndrome is a harbinger of death and should be proactively sought and energetically managed.

## Acknowledgements

We thank the dedicated efforts of all staff of our Medical College and Hospital in patient care and publication of this case report.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Guidelines for the Management of Snakebites. 2<sup>nd</sup> ed. New Delhi: WHO Regional Office for South-East Asia; 2016. Available from: <https://apps.who.int/iris/handle/10665/249547>.
2. Snake bite—the neglected tropical disease. *Lancet* 2015;386:1110.
3. Senji Laxme RR, Khochare S, Attarde S, Suranse V, Iyer A, Casewell NR, *et al.* Biogeographic venom variation in Russell's viper (*Daboia russelii*) and the preclinical inefficacy of antivenom therapy in snakebite hotspots. *PLoS Negl Trop Dis* 2021;15:e0009247.
4. Aneja R, Manaker S, Finlay G. Idiopathic systemic capillary leak syndrome. In: UpToDate [Last accessed on 2021 Oct 06].
5. Gutiérrez JM, Escalante T, Rucavado A, Herrera C. Hemorrhage caused by snake venom metalloproteinases: A journey of discovery and understanding. *Toxins (Basel)* 2016;8:93.
6. Thomas RG, Kumar J. Clinical features, prognostic factors and outcome of capillary leak syndrome in snake bite envenomation. *Int J Adv Res* 2016;4:2707-10.
7. Kandasamy S, Gopalakrishnan S, Venkatesan M, Ramakrishnan M. The clinical and biochemical profile of snakebite patients—A hospital based comparative study of envenomed and nonenvenomed victims. *Int J Biochem Biotechnol* 2014;3:511-5.
8. Gopalakrishnan N. Snake envenoming—An underreported cause of acute kidney injury. *Kidney Int Rep* 2019;4:643-6.
9. Udayabhaskaran V, Arun Thomas ET, Shaji B. Capillary leak syndrome following snakebite envenomation. *Indian J Crit Care Med* 2017;21:698-702.