

**Thrombotic microangiopathy in Hump nosed viper ‘Hypnale’ envenomation.**

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**Abstract**

Hump-nosed viper (HNV) which comprises ‘Hypnale hypnale’, ‘H. zara’ and ‘H. nepa’ is recognized as a highly venomous snake and ‘H. zara’ and ‘H. nepa’ are the commonest cause of snakebite envenoming in Sri Lanka. It has been earlier identified as resulting in only minor or local envenoming whereas, now known to cause serious systemic toxicity and fatalities. Here we report a case of 62 year old female presented with Hump-nosed viper bite who developed Microangiopathic Haemolytic anaemia (MAHA) and Acute Kidney Injury (AKI) which recovered spontaneously without residual renal or haematological abnormalities.

**Keywords**

Hump nosed Viper Envenomation, Microangiopathic Haemolytic Anaemia, Acute Kidney Injury

**Introduction**

Hump-nosed viper is now recognized as a highly venomous snake and it is the commonest cause of snakebite envenoming in Sri Lanka (1). There are three species of Hump-nosed vipers identified namely *Hypnale hypnale*, common to Sri Lanka and Western Ghats of peninsular India, and *H. nepa* and *H. zara* both of which are endemic to Sri

Lanka. *H. nepa* is restricted to the higher elevations of Sri Lanka and *H. zara* is widely distributed in the Island’s south western ‘wet-zone’ low lands (<600m). There is another un-named species (*Hypnale* sp. “Amal”), described from a single specimen collected near Galle in southern Sri Lanka (2). In Sri Lanka, this small pit viper is known as ‘polon-thelissa’ (viper with an upturned lip) or ‘kunakatuwa’ (referring to the necrotic effects at the bite site) in Sinhala, and ‘kopi viriyan’ (coffee snake) in Tamil. Hump-nosed viper bite was formerly identified as resulting in only minor or local envenoming whereas, now known to cause serious systemic toxicity and fatalities. Clinical manifestations of systemic envenoming by this snake include acute kidney injury, hematological manifestations, other organ involvement, and death in some cases. Several unusual manifestations have also been reported (1). Here we report a case of Microangiopathic Haemolytic anaemia and Acute Kidney Injury, rare complications of Hump-nosed viper envenomation.

**Case Presentation**

A 62 years old previously healthy lady from ‘Homagama’ a suburb in Colombo, Sri Lanka presented to the local hospital within four hours following a Hump nosed viper Bite in her home garden. The snake was confirmed as an HNV by a herpetologist. Even though her initial assessment

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**Table 1: The pattern of blood biochemical investigations from admission to discharge of patient**

Blood investigations	Units	Local Hospital	On Admission	Day 2	Day 4	Day 5	Day7	Day 10
White cell count (4000–11,000/mm <sup>3</sup> )		12,000	14,000	22,000	12,000	9,000	8,000	7,000
Neutrophils	%	73	65	73	67	65	64	68
Lymphocytes	%	20	32	24	21	23	32	25
Haemoglobin (11.5–13.5 g/dL)		100	85	80	81	95	110	120
Platelet (150,000–450,000/mm <sup>3</sup> )		250000	150	88	100	170	200	210
Serum Creatinine (17–107µmol/L)		100	295	490	400	210	112	110
Blood urea (<25mg)		30	54	68	65	45	32	25
Serum Sodium (135–145mmol/dL)		140	138	135	135	137	136	134
Serum Pottasium (3.5–5.0mmol/L)		4.5	5.0	5.3	4.9	4.3	4.8	4.1
Total bilirubin (0.3–1.6mg/dL)	-	-	-	28	22	16	15.0	2.0
Direct bilirubin (0.075–0.4mg/dL)	-	-	-	7.4	6.1	4.1	5.8	1.2
Indirect bilirubin (0.025–1.2mg/dL)	-	-	-	20.6	15.9	11.9	9.2	0.8
PT/INR (<1.4)	-	-	1.1	1.2	1.3	1.1	1.0	1.0
APTT (30–45 s)	-	-	32	34	32	35	34	32
AST (12–40 IU/L)	-	-	24	32	35	32	31	30
ALT (<40 IU/L)	-	-	32	40	35	32	35	32

was unremarkable and whole blood clotting test (WBCT) was normal, the next day WBCT was more than 20 minutes with deranged renal functions and oliguria. On admission, her vital parameters were stable with a Glasgow Coma Scale of 15/15 and a visible bite mark was observed over the medial aspect of the foot with features of cellulitis. Her initial blood investigations and subsequent investigations are shown in Table 1. Her blood picture showed fragmented red blood cells and thrombocytopenia suggestive of microangiopathic haemolytic anaemia which is shown Figure 1. She was closely monitored for clinical and biochemical evidence of deterioration of renal functions and adequate hydration and was maintained with oral fluids and Intravenous normal saline to prevent pre-renal-renal failure. Urine output was achieved with

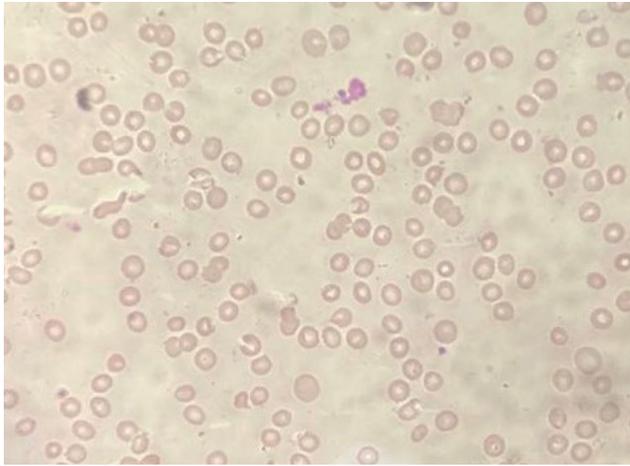
hydration and intravenous Furosemide therapy. Platelet count, Haemoglobin level and blood picture appearance of MAHA gradually improved over five days. Patient recovered without residual renal or haematological impairment.

### Discussion

Hypnale hypnale venom has had potent cytotoxicity with weak neurotoxicity, myotoxicity and procoagulant activity. Locally available polyvalent antivenom had not been capable of neutralizing any venom effect (3). The most commonly reported effects of Hump-nosed viper bite is local envenoming accounting for 90% of incidence which include local pain and swelling, local haemorrhagic blistering, regional lymphadenopathy and rarely severe local necrosis and gangrene. Systemic

effects include nephrotoxicity, coagulopathy, thrombocytopenia, spontaneous

**Figure 1:** Blood picture showed the fragmented red blood cells and mild thrombocytopenia suggestive of microangiopathic haemolytic anaemia



haemorrhage and non-specific symptoms such as headache, nausea, vomiting, and abdominal pain. Our patient showed haematological abnormalities and acute kidney injury evidenced by mild anemia, thrombocytopenia, microangiopathic haemolytic anaemia and oliguria with elevated serum creatinine level respectively (1). However, this patient did not require dialysis and her renal functions and haematological manifestations returned to normal spontaneously after several days. Sri Lankan H. hypnale venom L-amino acid oxidase, PLA<sub>2</sub>, and snake venom metalloproteases are recognised as having cytotoxic and tissue damaging properties leading to local envenomation whereas, snake venom serine proteases (thrombin-like enzymes) are responsible for venom-induced consumptive coagulopathy. C-type lectins are platelet modulators and they inhibit platelet aggregation, causing hemotoxic effect or potentiate platelet aggregation, which leads to thrombocytopenia (4). However, the nephrotoxic effect of the Hypnale venom remains unclear and may be due to renal hypoperfusion and ischemia caused by venom-induced consumptive coagulopathy (5).

Microangiopathic haemolytic anaemia (MAHA) is a well-known complication following viperidae snake bites, including Hump-nosed viper. The high amount of PLA<sub>2</sub> found in Hypnale venom may damage red blood cell lipid membranes, leading to intravascular hemolysis. MAHA is diagnosed when features of anemia (polychromatics and spherocytes), evidence of hemolysis, and the presence of fragmented red cells (>4 in ×100 field) are observed in peripheral blood smear. Hemolysis is evidenced by elevated indirect bilirubin and lactate dehydrogenase levels and decreased packed cell volume and serum haptoglobin level. We didn't measure haptoglobin levels in this patients due to the resource-poor setting, but hemolysis was evidenced by the blood picture (fragmented red cells, polychromatics, and spherocytes), reduction of hemoglobin, with elevated retic count, LDH and indirect bilirubin level (6).

With the available clinical data it appears that acute kidney injury sets in within the first 24–48 hours post bite and can manifest as oliguria, haematuria, proteinuria, pigmenturia (haemoglobinuria and myoglobinuria) and elevated serum creatinine level (7). Even though it is rare, there are several case reports which describe coagulopathy in association with acute kidney injury following Hump-nosed viper bite in Sri Lanka. High degree of clinical suspicion is needed for early detection of associated acute kidney injury and microangiopathic haemolytic anaemia in order to act timely to prevent complications and deaths among patients with Hump nosed Viper envenomation. This case report illustrates rare complication of HNV envenomation as TMA

which resolved spontaneously with supportive therapy.

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