Haemolytic Uremic Syndrome a Hitherto Unreported Complication of Humpnosed Viper Envenomation

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Abstract Merrem's humpnosed viper bite is known to cause incoagulable blood, acute renal failure, acute respiratory distress syndrome, Raynaud's phenomenon and gangrene of the distal limb. Venom-induced consumptive coagulopathy (VICC) is the commonest coagulopathy that occurs following snake envenomation which is characterised by prolonged clotting times. In a small proportion of patients with VICC, microangiopathy is also seen. The authors report a novel case of haemolytic uraemic syndrome following a merrem's humpnosed viper bite, which highlights the need for comprehensive and serial haematological evaluation to detect the condition and initiate timely plasma exchange. The authors recommend screening of all victims of humpnosed viper bite for haemolytic uremic syndrome which might otherwise be overlooked and stress the need for further studies to see the role of haemolytic uremic syndrome following humpnosed viper bite.

Keywords Humpnosed viper · Haemolytic uraemic syndrome · Acute kidney injury

Introduction

The authors report a novel case of haemolytic uraemic syndrome following merrem's humpnosed viper bite, a phenomenon which has not been documented to date in medical literature.

Case History

A 70 year old farmer got hospitalized 48 h after a Merrem's humpnosed viper—*Hypnale hypnale* (MHNV) bite with fever, cola coloured oliguria, and nausea. History was negative for alcoholism or prior medical conditions.

Examination revealed fever, periorbital oedema, pallor, icterus, and dependant oedema. Mucocutaneous bleeding, lymphadenopathy, stigmata of chronic liver disease were absent. The left shin had fang marks without evidence of local envenomation. Pulse and blood pressure were recorded at 110/min and 180/90 mmHg respectively. The jugular venous pressure was elevated. Precordium was normal. Respiratory, abdominal and neurological examination was unremarkable except for mild tachypnoea and flapping tremors.

Haematological tests showed—Haemoglobin 10.4 g/dl, 12 % reticulocytes, platelets—88,000/mm³, leucocytes—9,900/mm³ with 78 % neutrophils with marked red cell fragmentation and burr cells suggestive of microangiopathic haemolytic anemia (MAHA) on microscopy. Whole blood clotting time was normal. Lactate dehydrogenase (LDH) was elevated—2,000 IU/l. Urine strip testing showed haemoglobin and increased urobilinogen.

Serum creatinine and potassium were elevated at 600 µmol/l and 6.3 mmol/l respectively with normal

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sodium, liver enzyme and protein levels. Serum Total bilirubin was elevated—60 $\mu\text{mol/l}$ —with a predominantly elevated indirect fraction—47 $\mu\text{mol/l}$. Prothrombin time (PT) and activated partial thromboplastin time (APTT), D dimers were repeatedly normal. Coombs was negative. Ultrasound scan showed normal kidneys.

The patient received urgent plasma exchange (PE) and haemodialysis with packed cell transfusions.

Retrospective assessment excluded preceding diarrhoeal or febrile illness, blood transfusions, sexual promiscuity and clinical features suggestive of malignancy or hematological disease. Drug history was negative for quinine, antiplatelet agents, chemotherapeutic agents and immunosuppressants. HIV and antiphospholipid antibodies were negative.

He responded to PE with rapid improvement—after 4 sessions the platelet count rose to 245,000/ mm^3 and the LDH returned to baseline. Urine output improved with normalization of blood pressure and serum creatinine levels. Haemodialysis was discontinued after 5 sessions. He was discharged on the 10th day of hospitalization clinically well with near normal haematological and biochemical parameters. On subsequent clinic visits comprehensive clinical and laboratory assessment yielded unremarkable findings.

Discussion

The Merrem's hump-nosed viper (*Hypnale hypnale*) is an elapid endemic in India and Sri Lanka which is considered as moderately venomous compared with the more venomous endemic counterparts, namely the Russell's viper and the saw scaled viper.

Merrem's hump-nosed viper (MHNV) envenomation has been documented to cause a variety of clinical manifestations including incoagulable blood, acute renal failure, acute respiratory distress syndrome, Raynaud's phenomenon and gangrene of the distal limb [1, 2].

The commonest coagulopathy due to snake envenomation globally is venom-induced consumption coagulopathy (VICC), due to activation of the coagulation cascade by toxins in the venom—thrombin-like enzymes, prothrombin activators, and factor X activators. In a proportion of patients with VICC, thrombotic microangiopathy has been reported and is characterized by acute renal failure, thrombocytopenia, and microangiopathic hemolytic anemia. This thrombotic microangiopathy appears to only occur in conjunction with VICC in vipers and several other snakes. Consistent with thrombotic microangiopathy, it progresses despite the resolution of the coagulopathy, suggesting a distinct but related process [3].

In a study with 56 patients with proven hump-nosed viper (*Hypnale hypnale*) bites, 12 (21.4 %) developed continued oozing of blood from the site of the bite and a prolonged clotting time. Further investigations showed low fibrinogen levels and increased fibrinogen degradation products in plasma. The bleeding time, platelet count, prothrombin time, and partial thromboplastin time with kaolin were normal and the author concluded that excessive fibrinolysis seems to be the main abnormality [4].

Haemolytic uremic syndrome which is characterised by the absence of prolonged clotting times, occurring following MHNV envenomation has no precedence in medical literature.

Thrombotic microangiopathy is a microscopic description that is characteristic of several diverse disorders, such as malignant hypertension, DIC, scleroderma, thrombotic thrombocytopenic purpura (TTP) and HUS. When a patient presents with two or more of the following characteristic set of clinical and laboratory features sans alternate explanation HUS should be suspected [5]

1. MAHA
2. Thrombocytopenia
3. Acute renal impairment of varying severity
4. Neurological impairment
5. Fever

Even though renal impairment is a known feature of MHNV envenomation, thrombocytopenia and MAHA alone without another clinically apparent etiology are adequate to suspect HUS and commence PE [6]. The rapid clinical, haematological and biochemical response in our patient to PE further justifies the diagnosis of HUS.

AKI following MHNV envenomation has been pathophysiologically attributed to renal cortical necrosis in a study with limited post-mortem studies done on mortalities due to MHNV [2]. A necropsy study of HUS mortalities due to shigellosis showed cortical necrosis, extensive glomerular thrombosis or arterial thrombosis as the characteristic renal histological findings [7].

Untreated, HUS in adults results in irreversible renal failure, progressive neurologic deterioration, cardiac ischemia and death. Mortality rates are under 20 % in HUS patients treated with PE which is presently the most efficacious treatment.

Conclusion

This confirmed case of HUS following MHNV envenomation without documented precedence in literature is reported as an eye opener. Objective clinical studies are needed to evaluate the role of HUS contributing to the

overall morbidity and mortality after MHNV envenomation, to improve outcomes.

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