Type IV renal tubular acidosis following resolution of acute kidney injury and disseminated intravascular coagulation due to hump-nosed viper bite

S. Karunarathne, Y. Udayakumara, D. Govindapala, H. Fernando
Department of Clinical Medicine, National Hospital, Colombo, Sri Lanka

ABSTRACT

Hump-nosed viper bite can cause acute kidney injury (AKI) and disseminated intravascular coagulation. In some patients, it can cause chronic kidney disease necessitating life-long renal replacement therapy. Lack of effective antivenom makes the management of these patients difficult. A 51-year-old Sri Lankan male was admitted with AKI and disseminated intravascular coagulation following a hump-nosed viper bite. He made a complete recovery with blood product support and hemodialysis. Renal biopsy was performed as his renal recovery was prolonged which revealed patchy tubular atrophy and interstitial inflammation suggestive of subacute interstitial nephritis. Later, he presented with hyperkalemic paralysis and acidosis. A diagnosis of late onset type 4 renal tubular acidosis was made and he responded well to a course of fludrocortisone.

Key words: Snake bite, acute kidney injury, renal tubular acidosis

Introduction

Hump-nosed viper may account for upto 27-70% of all snake bites in Sri Lanka.[1,2] Although previously considered a moderately venomous, hump-nosed viper bites cause significant morbidity in the wet zone (hot and humid south western part of the island with an annual rainfall of more than 2,500 mm) of Sri Lanka. Acute kidney injury (AKI) necessitating hemodialysis and disseminated intravascular coagulation are known complications of hump-nosed viper bite.[2-8] The lack of an effective antivenom has contributed to the difficulty experienced by the clinicians during management of hump-nosed viper bites.[8]

We describe a patient who developed disseminated intravascular coagulation and prolonged AKI following a hump-nosed viper bite. He was successfully managed with hemodialysis and blood product support but he after developed severe hyperkalemia and acidosis due to type IV renal tubular acidosis after discharge from hospital. Type IV renal tubular acidosis has not been described previously in patients who had snake bites.

Address for correspondence:
Dr. Suneth Karunarathne, Registrar in General Medicine, National Hospital, Colombo, Sri Lanka.
E-mail: suneth871@gmail.com

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Case Report

A 51-year-old male was admitted to the local hospital after a hump-nosed viper bite on his hand while weeding his garden. Since the viper was brought alive by the neighbors, primary care physician was able to make a positive identification of the snake as Merrem's hump-nosed viper (*Hypnale hypnale*). The patient had severe pain and swelling in the hand. The next day his urine output was reduced and he was transferred to a tertiary care institute for hemodialysis. On admission, patient was conscious and rational, febrile, and he was in pain. He was pale and mildly icteric. He had marked swelling and redness in his right hand with blistering at the bite site.

His pulse rate was 92 beats per minute and blood pressure was 118/78 mmHg. On auscultation of the heart, S1 and S2 were heard in normal intensity with no murmurs. Respiratory system examination was normal except for few fine basal crepitations. Abdominal

examination was normal with no organ enlargement or free fluid. Neurological examination was normal with no ophthalmoplegia or other cranial nerve paralysis.

His investigation results were as follows: white cell count, 12,700 (80% neutrophils); platelet count, 40,000/μl; hemoglobin, 9.9 g/dl; International normalized ratio, 1.46; activated partial thromboplastin time, 43 s; serum creatinine, 1,040 μmol/l; Na, +130 mmol/l; K+, 5.4 mmol/l; erythrocyte sedimentation rate, 10 mm/Hr; C-reactive protein, 1 mg/L; aspartate transaminase, 54 u/l; alanine transaminase, 42 u/l; serum bilirubin, 22.7 μmol/l; total protein, 52 g/l (albumin 33 g/l). Peripheral blood smear revealed marked red cell fragmentation, polychromasia and reduced number of platelets indicating disseminated intravascular coagulation. Serum calcium, 7.7 mg/dl; serum phosphate, 3.1 mg/dl; creatine phosphokinase, 122 u/l; urine microscopy showing 10-12 pus cells and 1-2 red cells per high power field with no casts. Protein was present in urine in trace amounts. Abdominal ultrasound scan revealed enlarged and globular kidneys suggestive of acute renal parenchymal disease. Venom-induced acute tubular necrosis was suspected.

He was commenced on hemodialysis. After 12 sessions of hemodialysis, he was dialysis dependent and renal biopsy was performed 8 weeks after the viper bite. The biopsy revealed patchy areas of tubular atrophy with interstitial edema and patchy interstitial chronic inflammation suggesting subacute interstitial nephritis. There was no evidence of acute tubular necrosis possibly because biopsy was performed very late after the onset of AKI. Glomeruli were normal.

Ten weeks after the viper bite, the patient's renal functions and urine output were improved. He was discharged from the hospital to be reviewed in clinic as an outpatient. At the time of discharge, he had a serum creatinine of 1.9 mg/dl and serum potassium of 3.9 mmol/l.

Eighteen weeks after the initial viper bite, he was admitted with sudden onset bilateral lower limb weakness. There was no respiratory muscle paralysis. Both lower limbs had grade two muscle power and upper limbs grade four. Reflexes were diminished and Babinski sign was negative. There was no objective sensory loss.

During this admission, he was found to have acidotic breathing. Arterial pH was 7.31 and PCO_2 18 mmHg, PO_2 121 mmHg, and HCO_3^- 10.3 mmol/l. His serum potassium level was 7.0 mmol/l with sodium 130 mmol/l and chloride 114 mmol/l. ECG showed tall tented T waves suggestive of hyperkalemia. Serum creatinine was 114 μmol/l with an estimated glomerular filtration rate of 76 ml/min. He was given intravenous calcium gluconate, nebulized with salbutamol and started on insulin-dextrose infusion until an urgent hemodialysis was arranged. There was no history of use of angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), or diuretics like spironolactone.

Blood anion gap was normal at 5.7 mmol/l. Urine pH was 5.0. Urinary electrolytes were as follows: Na^+ 77 mmol/l, K^+ 16 mmol/l, Cl^- 84 mmol/l, pH 5.0, serum osmolality 300 mosm/kg, urine osmolality 380 mosm/kg, and urinary anion gap was 9 mmol/l. Transtubular potassium gradient (TTKG) was 1.80.

Presence of hyperchloremic metabolic acidosis and hyperkalemia with normal serum creatinine level was suggestive of type IV renal tubular acidosis. The ability to lower the urine pH to 5.0, positive urinary anion gap, and the low TTKG (less than five) were all supportive evidence for type 4 renal tubular acidosis.

Patient had a good response to fludrocortisone 100 μg twice daily with the correction of hyperkalemia and the metabolic acidosis. He was discharged while on fludrocortisone with serum potassium of 4.3 mmol/l. Three weeks later, fludrocortisone was stopped as serum potassium was 3.5 mmol/l and he was closely observed for the development of hyperkalemia or acidosis. Eight weeks after discharge, he had potassium of 4.2 mmol/l without any potassium-lowering drug therapy.

Discussion

Type 4 renal tubular acidosis is due to failure of the collecting duct to excrete both potassium and protons. This is caused by absolute or functional deficiency of aldosterone or a molecular defect in the relevant transporters. Aldosterone is necessary for the maintenance of the lumen negative potential by the reabsorption of Na^+ by the epithelial sodium channel on the luminal membrane of the principal cells. This lumen negative potential in turn drives the secretion of potassium and protons into the lumen.[9] This subtype of renal tubular acidosis is usually observed in patients with diabetes mellitus and various forms of tubulointerstitial disease including sickle cell disease, amyloid, monoclonal gammopathy, and NSAID-induced interstitial nephritis. Drugs that cause a similar picture include ACEI, ARB spironolactone, heparin,[10] and β-blockers.[11] These causes were excluded in this patient.

The possible pathogenesis of renal tubular acidosis in this

patient could be due to snake venom-mediated tubular damage leading to aldosterone receptor dysfunction or aldosterone resistance. The favorable response to fludrocortisone supports this hypothesis.

Conclusions

Although disseminated intravascular coagulation necessitating blood product support and AKI are known complications of hump-nosed viper bite, the development of type 4 renal tubular acidosis was a new finding.

This case is clinically informative because it describes a previously unknown complication following viper bite and makes a clinician more vigilant regarding renal function and serum electrolyte levels even after patient has recovered from snake venom-induced AKI.

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