Renal tubular dysfunction presenting as recurrent hypokalemic periodic quadriparesis in systemic lupus erythematosus

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ABSTRACT

We report recurrent hypokalemic periodic quadriparesis in a 30-year-old woman. Patient had also symptoms of multiple large and small joint pain, recurrent oral ulceration, photosensitivity and hair loss that were persisting since last 6 months and investigations revealed systemic lupus erythematosus (SLE) with distal tubular acidosis. Our patient was successfully treated with oral potassium chloride, sodium bicarbonate, hydroxychloroquine and a short course of steroids. Thus, tubular dysfunction should be carefully assessed in patients with SLE.

Key words: Distal renal tubular acidosis, hypokalemic periodic quadriparesis, renal tubular dysfunction, systemic lupus erythematosus

Introduction

Hypokalemic periodic paralysis is a rare disorder characterized by transient attacks of flaccid paralysis of varying intensity and frequency. Reported incidence of hypokalemic paralysis in patients with type 1 renal tubular acidosis (RTA) is about 28-53% respectively.[1] Type 1 RTA or distal RTA (dRTA) is a disorder of renal tubular acidification characterized by hyperchloremic metabolic acidosis with a normal serum anion gap. dRTA can be inherited or acquired.[2,3] Inherited forms include autosomal-dominant, autosomal-recessive, or X-linked recessive, of which autosomal-dominant form causing mutations in the basolateral chloride bicarbonate exchanger (AE1) has been identified as the most common form of inheritance. Acquired causes include hypergammaglobulinemic states, such as hyperglobulinemic purpura, cryoglobulinemia, fibrosing alveolitis, Sjogren syndrome, lupus, chronic active hepatitis, thyroiditis, Graves' disease, primary biliary cirrhosis; disorders of calcium metabolism, e.g. primary hyperparathyroidism, vitamin D intoxication, idiopathic hypercalciuria, familial absorptive hypercalciuria, medullary sponge kidney.[4,5] Renal involvement in systemic lupus erythematous is mainly glomerulonephritis and isolated tubular dysfunction is rare. This unusual presentation of systemic lupus erythematosus (SLE) was first presented by Fortenberry and Kenney in 1991[6] and infrequent cases have been reported in the literature ever since. We present the case of a woman who was admitted with acute onset hypokalemic quadriparesis. Investigations revealed underlying dRTA. Six months after the initial presentation, the patient fulfilled 5 out of 11 American College of Rheumatology (ACR) criteria for diagnosis of SLE[7] and patient was managed successfully with oral and intravenous potassium chloride, sodium bicarbonates and oral hydroxychloroquine and a short course of steroid.

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Access this article online	
Quick Response Code:	Website: www.indianjnephrol.org
	DOI: 10.4103/0971-4065.133019

Case Report

A 30-year-old woman presented with gradually increasing weakness of both upper and lower limbs. She reported having had a similar episode twice previously, most recently 2 months ago; and at all of these occasions, she had documented hypokalemia and she was managed by

a local physician with parenteral and oral administration of potassium chloride that improves her condition on these occasions. Resting after exercise or eating did not precipitate the weakness and there was no family history of similar illness. Patient also had complaints of recurrent oral ulceration, photosensitivity, hair loss, loss of appetite, easy fatigability, pain in multiple joints and she experienced this pain almost throughout the day, but it was worse in the morning. The patient also had significant morning stiffness and daytime fatigue. All these symptoms were present since 6 months. She had also off and on low grade fever over 3 months before admission but she had no burning in the urine, cough and abdominal pain or vomiting, pruritus, dryness of mouth, difficulty in swallowing, gritty or sandy sensation under eyelids and Reynaud's phenomenon. On the day of admission, the patient also complained of difficulty in swallowing solid food and inability to speak loudly but there was no history of visual blurring, diplopia, facial asymmetry, sensory, bladder, or bowel complaints. She had a clear sensorium with no history of seizures, involuntary movements, root pains, or band-like sensation over the trunk. She did not give a history of prior drug intake, colicky abdominal pain and recent vaccination.

Six months before her current presentation, the patient had progressive weakness in all four limbs; it started in one limb, but progressed to all four limbs within a few hours and her past medical record and history given by her husband revealed that she was conscious and oriented at the onset of weakness. Her eye movements were normal and there was no facial asymmetry and seizure at the onset of weakness. At current admission to our hospital in physical examination, blood pressure was 130/80 mm Hg; Pallor was present. There was no edema, icterus and lymphadenopathy. Musculoskeletal and neurological examination revealed muscle strength was poor (flicker 1/5) in all the muscle groups. Deep tendon reflexes were intact and planter reflex was flexor bilateral. Laboratory investigations done revealed blood urea 28 mg/dl, serum creatinine 1.3 mg/dl, hypokalemia 2.2 mmol/L, hyperchloremic metabolic acidosis (chloride 112 mEq/L, arterial blood pH 7.279) and alkaline urine (urinary pH 7.5). Radiograph of the abdomen did not show any nephrocalcinosis. Ultrasonography of the abdomen revealed right nephrolithiasis with bilateral normal size kidney and normal liver size and echotexture. In view of the normal anion gap acidosis (12.4 mmol/l), alkaline urine (urinary pH 7.5), low serum potassium (2.2 mmol/l), absence of Fanconi's syndrome, positive urinary anion gap (46 mmol/l), the diagnosis of dRTA was made. Type 2 RTA was excluded, as her 24 h urinary excretion of phosphate and uric acid was normal with no glycosuria. Renal biopsy was deferred in view of normal renal function and no active sediment in urine routine microscopy. The patient was started on oral potassium and bicarbonate supplementation. Oral hydroxychlroquine and a short course of steroid were also given. Her biochemical parameters corrected with treatment and she attained blood urea of 24 mg/dl, serum creatinine 1.0 mg/dl, potassium 3.9 mEq/L, chloride 95 mEq/L and arterial blood pH of 7.332. She had continued on the oral supplements with sodium bicarbonate (500 mg twice daily) and oral hydroxychloroquine 200 mg twice a day and had been asymptomatic on regular follow-up [Table 1].

Discussion

Our patient initially presented with generalized weakness and was diagnosed dRTA due to SLE on evaluation. Generalized weakness is a very subjective feeling and is an uncommon objective finding in outpatients and emergencies. There is a large differential diagnosis for muscle weakness, but only a few medical conditions develop rapid onset generalized muscle weakness. On initial presentation, we kept the possibility of inflammatory myopathy, thyroid disorder, channelopathy and neuropathy and electrolyte disturbance as the cause of our patient symptoms. We investigated our patient according to our differential diagnosis. Investigations revealed that patient did not have inflammatory myopathy as she had normal creatine phosphokinase and serum lactate dehydrogenase. Her liver function test and thyroid function test were normal. Rheumatoid factor test was negative and direct coomb's test was positive. Tests for human immunodeficiency virus hepatitis B and C were negative. She was diagnosed SLE based on ACR criteria for diagnosis of SLE[7] and dRTA on the basis of hyperchloremic metabolic acidosis, hypokalemia with a positive urinary anion gap and the absence of Fanconi's syndrome. Our case is considered to be an acquired form of dRTA with predominant tubular involvement in SLE. In dRTA, the kidney is not able to adequately excrete an acid (H+) load and loses its normal acid-base balance and characterized by hyperchloremic metabolic acidosis, a normal serum anion gap, a urinary pH ≥5.5, hypokalemia, a positive urinary anion gap, nephrolithiasis and daily replacement of sodium bicarbonate ≤4 mmol/kg generally improve the conditions.[8] Previous studies have also shown the association of SLE with various tubular defects,[9,10] dRTA being the most common type of tubular involvement in SLE, although type 4 RTA has also been recently reported.[11] Tubular dysfunction is well-described in SLE and coincides with active proliferative glomerulonephritis,[12] although patients usually show manifestations of lupus rather than features

Table 1: Hematological and biochemical parameters of patient

Parameters	Patient's values (normal range)
Hemoglobin (g/dl)	7.9 (12-18)
Total leucocyte count	4600 (4000-11,000/cumm)
DLC	N70 L26 E2
Platelets	34,000 (150,000-450,000/cumm)
ESR (per hour)	52 (<20)
Urea (mg/dl)	28 (15-45)
Serum creatinine	1.3 (0.6-1.6)
Calcium (mg/dl)	8.9 (9-11)
Phosphorus (mg/dl)	4.2 (2.5-4.5)
Alkaline phosphatase (IU/l)	112 (25-140)
Sodium (mEq/L)	137 (135-145)
Potassium (mEq/L)	2.2 (3.5-4.5)
Chloride (mEq/L)	112 (95-105)
ANA	1:80
Anti-dsDNA	176 (<35)
Rheumatoid factor	Negative
Direct Coomb's test	Positive
Bilirubin (mg/dl)	0.5 (<1)
SGOT (U/l)	23 (0-40)
SGPT (U/l)	30 (0-40)
Serum albumin (g/dl)	3.8 (3.5-5.0)
C3 (mg/dl)	72 (40-120)
C4 (mg/dl)	25 (10-40)
fT3 (pg/ml)	3.6 (2.3-4.2)
fT4 (ng/l)	1.2 (0.8-1.8)
TSH (μIU/ml)	5.0 (0.5-4.70)
LDH (U/l)	356 (160-420)
CPK (mcg/l)	34 (10-120)
Urine pH	7.5 (<5)
Sp. gravity	1.030
Urine protein	+
Urine RBC	Nil
Urine WBC	Nil
24 h urinary protein (g/day)	0.12 g/day
Urinary glucose	Negative
Urinary sodium excretion (mEq/day)	246 (40-220)
Urinary K excretion (mEq/day)	55 (25-120)
Urinary chloride excretion (mEq/day)	255 (110-150)
Urinary calcium excretion (mg/day)	190 (50-150)
Urinary phosphate excretion (mg/day)	614 (400-1300)
Urinary uric acid excretion (mg/day)	350 (250-750)
Arterial blood gas analysis	
pH	7.279
PCO_2	36
PO_2	88
HCO_3	12.6
SpO_2	98

DLC: Differential leukocyte count, ESR: Erythrocyte sedimentation rate, ANA: Antinuclear antibody, Anti-dsDNA: Anti-double-stranded DNA antibodies, C3: Complement 3, C4: Complement 4; fT3: Free triiodothyronine, fT4: Free thyroxine, TSH: Thyroid stimulating hormone, SGPT: Serum glutamate pyruvate transaminase, SGOT: Serum glutamic oxaloacetic transaminase, RBC: Red blood cell, WBC: White blood cell, LDH: Lactate dehydrogenase, CPK: Creatine phosphokinase

of RTA. The exact mechanism of tubular damage is not known. Pasternack and Linder found the deposition of immunoglobulin with complement as well as immunoglobulin-producing mononuclear cells around the tubuli, which was highly suggestive of an immunological process affecting the tubuli, eventually leading to the destruction of some of them.[13] To conclude, tubular function should be assessed carefully in lupus patients and a work-up for the presence of SLE should be done in all RTA cases.

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How to cite this article: Prasad D, Agarwal D, Malhotra V, Beniwal P. Renal tubular dysfunction presenting as recurrent hypokalemic periodic quadriparesis in systemic lupus erythematosus. Indian J Nephrol 2014;24:315-7.

Source of Support: Nil, **Conflict of Interest:** None declared.