CASE REPORT

Hypokalemia Secondary to Distal Renal Tubular Acidosis as a Manifestation of Primary Sjögren Syndrome

CHINNASWAMI VIJAIKUMAR*, UDHAYA BALASUBRAMANIAN†, TAMILSELVAN RAMASAMY‡

ABSTRACT

The classical symptoms of primary Sjögren syndrome such as dry eyes and mouth are not always the initial manifestations. Herein, we report the case of a middle-aged female with documented multiple hypokalemic paralytic episodes along with nonspecific symptoms. Upon evaluation, she was found to have type 1 – distal renal tubular acidosis (RTA), which is an extraglandular manifestation of Sjögren syndrome. She was administered oral alkali salts of sodium along with potassium citrate and oral prednisolone. Both hypokalemia and acidosis recovered on 6th week follow-up. She was advised to continue alkali supplementation.

Keywords: Hypokalemic paralysis, urine anion gap, type 1 distal RTA, RTA, primary Sjögren syndrome

Primary Sjögren syndrome is a common chronic autoimmune disease characterized by lymphocytic infiltration of exocrine glands, mainly salivary and lacrimal, resulting in oral and ocular dryness, although virtually any organ system can be affected[1]. Extraglandular manifestations of Sjogren's syndrome include palpable purpura, interstitial lung disease, distal renal tubular acidosis (RTA); membranoproliferative glomerulonephritis and peripheral neuropathy[2]. Clinical renal disease is unusual in primary Sjögren syndrome, being reported in 5% of patients, but it is probably underestimated. Chronic tubulointerstitial nephritis is the predominant form of primary Sjögren syndrome-associated renal involvement, which clinically translates mostly into distal RTA[2].

Furthermore, type 1 distal RTA is characterized by a cortical collecting duct dysfunction leading to an impaired elimination of hydrogen (H^+) ion. Secondary to tubular defects, patients develop systemic metabolic acidosis or the inability to acidify urine following an oral acid intake. Weakness or paralysis due to hypokalemia, renal calculi, or osteomalacia may be present in primary Sjögren syndrome patients with distal RTA[2].

CASE REPORT

A 45-year-old female presented with complaints of generalized weakness and tiredness since 5 years. She had generalized muscle pain over hands and legs for the past 4 years along with tingling and numbness for past 9 months. She also gave a history of occasional cough for 15 years and oral ulcers for past 1 year. She had no co-existing comorbid illness and there were no symptoms such as chest pain, palpitation, loss of weight or appetite, decreased urine output, shortness of breath or excessive menstrual flow. She had a history of recurrent hypokalemia paralytic attacks for past 3 years, which was not evaluated for the cause. She was not on any diuretics or other potassium-lowering drugs. Physical examination was normal except for oral ulcers and dry eyes. Skin and joint movements were normal. She ate the usual Indian diet. Vitals were stable and neurological examination was unremarkable.

Her complete blood count (CBC) was normal with hemoglobin of 13.9 g/dL, total white blood cell counts of 7,140 cells/mm^3 with normal differential counts; platelet count of 3,45,000; erythrocyte sedimentation rate (ESR) at 1 hour was 26 mm. Renal and liver function parameters were normal. Serum electrolyte

*Senior Consultant, Dept. of General Medicine
†National Advisor, Dept. of Preventive Medicine
‡Post Graduate
Apollo Hospitals, Greams Road, Chennai, Tamil Nadu, India
Address for correspondence
Dr Tamilselvan Ramasamy
Apollo Hospitals, Greams Road, Chennai, Tamil Nadu, India
E-mail: tamilselvan.r.cbe@gmail.com

assay showed hypokalemia 2.7 mEq/L (normal range 3.5-4 mEq/L); low serum bicarbonate 19 mEq/L (normal range 22-26 mEq/L); normal serum sodium 139 mEq/L and mildly raised serum chloride 112 mEq/L (normal range 98-107 mEq/L). Fasting thyroid-stimulating hormone (TSH) levels were normal 1.3 μIU/mL. Serum total vitamin D was deficient at 17.2 ng/mL (Table 1).

Urine routine examination showed pH of 7.5 with trace proteinuria without glucosuria or hematuria or sterile pyuria. The 12-lead electrocardiogram was normal with sinus rhythm and heart rate of 87 beats per minute with no T-wave morphological changes. 2D echocardiogram was normal with no regional wall motion abnormality or valvular pathology. Except for oral ulcers with dry eyes and hypokalemia with acidosis, the patient did not have any other pathology.

Table 1. Investigations Done for the Patient

Parameter	Patient's value	Normal value
Hemoglobin	13.9 g/dL	12-16 g/dL
White cell count	7,140/mm^3	4,000-11,000/mm^3
Platelet count	345 10^3/mm^3	150-450 10^3/mm^3
Neutrophils	45	40-80
Lymphocytes	44	20-40
Eosinophils	6	1-6
Monocytes	4	2-10
Blood urea	19 mg/dL	13-43 mg/dL
Serum creatinine	0.7 mg/dL	0.7-1.3 mg/dL
Alanine transaminase (ALT)	27 U/L	<34 U/L
Aspartate transaminase (AST)	30 U/L	<31 U/L
Alkaline phosphatase (ALP)	174 U/L	<141 U/L
Gamma-glutamyl transpeptidase (GGTP)	29 U/L	<38 U/L
Total bilirubin	0.8 mg/dL	0.0-1.3 mg/dL
Direct bilirubin	0.2 mg/dL	0.0-0.5 mg/dL
Indirect bilirubin	0.6 mg/dL	0-1.2 mg/dL
Serum albumin	4.2 g/dL	3.5-5.2 g/dL
Serum globulin	4.0 g/dL	2.0-3.5 g/dL
Serum sodium	139 mEq/L	136-145 mEq/L
Serum potassium	2.7 mEq/L	3.5-5.1 mEq/L
Serum chloride	112 mEq/L	98-107 mEq/L
Serum bicarbonate	19 mEq/L	22-26 mEq/L
Vitamin D Total	17.2 ng/mL	>30 ng/mL

She was having normal anion gap metabolic acidosis with hypokalemia and history of hypokalemic paralytic attacks. As she did not have any gastrointestinal causes of bicarbonate loss such as diarrhea and normal serum magnesium levels (1.55), urine electrolytes were done to evaluate renal losses. Spot urine sodium was 63.9 mmol/L; spot urine potassium was 32 mmol/L (normal range 17-80 mmol/L); spot urine chloride was 90 mmol/L (normal range 46-168 mmol/L); and spot urine creatinine was 49.53 mg/dL.

Urine anion gap, which is an indirect measure of urinary ammonium excretion, is calculated by the formula: Urine anion gap = (urine sodium + urine potassium) – urine chloride. In normal healthy individuals with no renal pathology, the urine anion gap is negative. Application of the above-mentioned formula to this patient yielded a positive urine anion gap of 6 mmol/L. Positive urine anion gap is suggestive of failure of urine acidification. Hence, a provisional diagnosis of RTA was made. Hypokalemia is present in type 1 (distal) and type 2 (proximal) RTA. Patient tested strongly positive for SSA (Ro) and Ro-52 antibodies (Table 2). With normal calcium, magnesium, and phosphorous levels, a final diagnosis of type 1 distal RTA secondary to Sjögren syndrome was made. Urinary potassium creatinine ratio was suggestive of renal potassium loss. Renal biopsy is not mandatory, and since our patient had normal renal function, it was not performed.

Treatment was started with oral sodium bicarbonate 1 g thrice daily, potassium citrate, oral vitamin D/calcium supplementation, and oral prednisolone 50 mg (tapering dose weekly). On a 6-week follow-up, serum electrolytes were rechecked. Serum bicarbonate levels were - 22.4 mEq/L; serum potassium - 4.1 mEq/L. There were no abdominal or neurological symptoms from initiation of treatment till follow-up. She was advised to continue potassium citrate and dosage of oral sodium bicarbonate reduced to 500 mg twice daily.

Table 2. Extractable Nuclear Antigens (ENA)-7 IgG Panel by IMMUNOBLOT Technique

Anti-Sm	Negative
Anti-Sm/RNP	Negative
SSA (Ro)	Strongly positive 3+
Anti-Ro-52	Strongly positive 3+
SSB (La)	Negative
Scl-70	Negative
Anti-Jo-1	Negative

DISCUSSION

Sjögren syndrome is an autoimmune disease characterized by chronic lymphocytic infiltration of exocrine glands resulting in clinical manifestations such as xerostomia, dry eyes[1]. The extraglandular manifestations of primary Sjögren syndrome are usually less frequent but can affect virtually any organ. They can occur at presentation or during the course of primary Sjögren syndrome, and if present can impact prognosis[3]. Renal involvement is estimated to occur in up to 10% of patients, more frequently as tubulointerstitial nephritis (TIN) and rarely as glomerulonephritis[4]. TIN is manifested as distal RTA, nephrogenic diabetes insipidus, proximal tubular dysfunction, normally without renal failure. Distal RTA is the most frequent renal manifestation, it is incomplete when there is a urinary acidification defect with normal serum bicarbonate and pH, and complete when there is a urinary acidification defect, low serum bicarbonate and acidosis[5]. Most laboratories cannot measure urinary ammonium; therefore, estimations can be made from urinary anion gap or osmolar gap. Positive urinary anion gap suggests reduced urine ammonium excretion, reflecting a primary defect in distal urine acidification, which characterizes distal RTA[4]. Despite being an extraglandular manifestation, distal RTA is not an indication for immunomodulatory therapy in primary Sjögren syndrome. However, steroid therapy can be considered when replacement therapy alone is unable to correct the imbalances, and in cases of recurring hypokalemic paralysis episodes. Early diagnosis and life-long alkali supplementation can prevent both acute hypokalemia and chronic complications like osteomalacia, renal stones, and progression to chronic kidney disease[4].

Metabolic acidosis also leads to enhanced proximal tubular reabsorption of citrate, resulting in hypocitraturia. Alkaline urine in combination with hypocitraturia and hyperphosphaturia promotes calcium phosphate precipitation leading to nephrocalcinosis and/or kidney stones[6]. The pathophysiological mechanism of distal RTA in relation to autoimmunity remains unclear. Several reports suggest that autoantibodies against the carbonic anhydrase enzyme[7].

Correction of the metabolic acidosis is by starting alkali in amount slightly greater than daily acid production. Correction of acidosis with sodium salts of such as sodium bicarbonate, can further aggravate hypokalemia. So, potassium supplementation should begin even before acidosis correction[8]. IgG4-related disease is often confused with Sjogren's syndrome, as the former can similarly affect the lacrimal and salivary glands, and present with tubulointerstitial nephritis[9].

CONCLUSION

Currently, there is no universal agreement on the diagnostic criteria for the diverse spectrum of extraglandular involvement in primary Sjögren's syndrome. This leads to significant underdiagnosis of extraglandular manifestations, resulting in inadequate treatment and progression to severe organ dysfunction in affected individuals[2]. It is crucial to establish correlations between the nonspecific presentations of systemic autoimmune diseases and initiate timely treatment to mitigate chronic debilitating outcomes.

Declaration

Funding: None.

Patient's Consent: Telephonic consent was obtained from the patient for research purposes.

Conflict of Interest: None.

Ethical Approval: Not required.

REFERENCES

1. Mavragani CP, Moutsopoulos HM. Sjögren's syndrome: Old and new therapeutic targets. J Autoimmun. 2020;110:102364.
2. Mihai A, Caruntu C, Jurcut C, Blajut FC, Casian M, Opris-Belinski D, et al. The spectrum of extraglandular manifestations in primary Sjögren's syndrome. J Pers Med. 2023;13(6):961.
3. Mariette X, Criswell LA. Primary Sjögren's syndrome. N Engl J Med. 2018;378(10):931-9.
4. Garza-Alpirez A, Arana-Guajardo AC, Esquivel-Valerio JA, Villarreal-Alarcón MA, Galarza-Delgado DA. Hypokalemic paralysis due to primary Sjögren syndrome: case report and review of the literature. Case Rep Rheumatol. 2017;2017:7509238.
5. Evans R, Zdebik A, Ciurtin C, Walsh SB. Renal involvement in primary Sjögren's syndrome. Rheumatology (Oxford). 2015;54(9):1541-8.
6. Both T, Zietse R, Hoorn EJ, van Hagen PM, Dalm VA, van Laar JA, et al. Everything you need to know about distal renal tubular acidosis in autoimmune disease. Rheumatol Int. 2014;34(8):1037-45.
7. Takemoto F, Hoshino J, Sawa N, Tamura Y, Tagami T, Yokota M, et al. Autoantibodies against carbonic anhydrase II are increased in renal tubular acidosis associated with Sjogren syndrome. Am J Med. 2005;118(2):181-4.
8. Palmer BF, Kelepouris E, Clegg DJ. Renal tubular acidosis and management strategies: a narrative review. Adv Ther. 2021;38(2):949-68.
9. Maślińska M, Przygodzka M, Kwiatkowska B, Sikorska-Siudek K. Sjögren's syndrome: still not fully understood disease. Rheumatol Int. 2015;35(2):233-41.