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Primary Sjögren's syndrome presenting with hypokalemic periodic paralysis: A case series

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ABSTRACT

Tubulointerstitial nephritis (TIN) is the primary renal involvement associated with primary Sjögren's syndrome (pSS). We present a series of female patients with hypokalemic paralysis due to distal renal tubular acidosis. The patients received symptomatic treatment, including potassium supplementation, with favorable responses. The evidence suggests an underlying inflammatory mechanism that can lead to serious complications such as hypokalemic paralysis. Based on our findings, a combination of potassium supplementation and corticosteroid therapy is suggested for managing pSS-associated TIN.

Key words: Distal renal tubular acidosis; Hypokalemic paralysis; Sjögren's syndrome; Tubulointerstitial nephritis

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INTRODUCTION

Sjögren's syndrome (SS) is a systemic autoimmune connective tissue disorder characterized by lymphocytic infiltration of exocrine glands, leading to xerophthalmia and xerostomia.[1] SS can be classified as either primary SS (pSS), occurring independently, or secondary, associated with autoimmune conditions such as rheumatoid arthritis, systemic lupus erythematosus (SLE), polymyositis, and systemic sclerosis. Although dry eyes and dry mouth are hallmark features, extraglandular manifestations are present in 75% of pSS cases.[2] Diagnosis relies on clinical features and laboratory findings, with the 2016 ACR/EULAR classification criteria being the latest diagnostic standard.[3] This strong criterion is the weighted average of five objective factors, including tests for objective ocular and oral dryness (two ocular tests, including Schirmer's test, and an oral test, each scoring one point), anti-Ro/SSA positivity, lymphocytic sialadenitis on salivary gland biopsy, with a focus score of 1 foci/mm^3, and both. An individual with either ocular or oral dryness with a score of <4 points is diagnosed with SS.

Renal involvement in pSS primarily manifests as tubulointerstitial nephritis (TIN), with distal renal tubular acidosis (dRTA) being the most common presentation.[4] dRTA, characterized by impaired hydrogen ion excretion, can lead to hypokalemic paralysis, a rare but severe complication. Approximately 7% of pSS patients present with hypokalemic paralysis as the first symptom.[5]

This case series describes pSS-associated TIN presenting as dRTA and highlights the demographic, biochemical, immunological, and clinical characteristics of these

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cases, along with their response to immunosuppressive therapy.

CASE 1

A 50-year-old female presented to the emergency department with acute-onset flaccid paralysis affecting all four limbs since the previous day. She initially experienced weakness in the right lower limb 2 days prior, which progressed to involve the right upper limb and, subsequently, all four limbs. There was no history of steroid or diuretic use preceding fever, diarrhea, or animal bites. No autonomic or sensory involvement was noted. She also had no history of renal stones, fractures, or similar complaints in the past.

On examination, she was afebrile, hemodynamically stable, and fully conscious and oriented. There was no evidence of goiter, parotid, or lacrimal gland enlargement. The neurological assessment revealed reduced muscle power (2/5) in all four limbs, bilateral plantar extensor responses, and diminished deep tendon reflexes (+1 in all four limbs). Sensory examination was unremarkable, cranial nerve functions were intact, and there were no speech disturbances or facial deviations.

Laboratory investigations revealed hypokalemia (serum potassium: 2.5 mEq/L) with normal serum sodium levels (149 mEq/L). Arterial blood gas (ABG) analysis indicated metabolic acidosis with a urine pH of 6.9. Urinary electrolyte analysis demonstrated significant potassium loss (urinary potassium: 276 mEq/L; normal range: 22–164 mEq/L), normal anion gap (11.9 mEq/l), and a urine anion gap of 20.6 mEq/L, suggestive of renal tubular acidosis. Electrocardiography (ECG) showed ST depressions with shallow and broad T waves.

Further immunological evaluation revealed a positive antinuclear antibody (ANA) profile with SS-A and Ro52 antibodies. Although the patient did not report symptoms of dry mouth or facial swelling, these findings were highly suggestive of SS. Schirmer's test confirmed severe ocular dryness (<4 mm wetting in 5 min in the right eye and <8 mm in the left eye).

The patient was treated with intravenous potassium and potassium citrate syrup, leading to rapid clinical improvement. By the following day, she was able to walk. She was subsequently discharged on potassium and bicarbonate supplementation along with low-dose corticosteroids. Follow-up evaluations demonstrated continued clinical improvement.

CASE 2

A 42-year-old female presented with complaints of vomiting, nausea, and decreased appetite, along with progressive weakness in all four limbs, resulting in difficulty walking and performing routine activities. Further evaluation revealed a history of easy fatigability, intermittent mild-grade fever, and a dry cough persisting for 6 months. There was no significant past medical or drug history, nor any history of weight loss or evening rise in fever.

On examination, the patient had hypotension (blood pressure: 100/60 mmHg) with pallor and dental caries. There was no evidence of goiter, parotid, or lacrimal gland enlargement. The neurological assessment revealed reduced muscle tone and power (3/5) in all four limbs, with no sensory deficits. Cranial nerve functions were intact, and there were no speech disturbances or facial deviations. ECG findings included flat T waves and ST segment sagging.

Laboratory investigations demonstrated persistent hypokalemia, hypocalcemia, and hypophosphatemia, along with decreased serum uric acid levels. Urine analysis revealed a pH of 8.4, significant proteinuria (albumin+4), and elevated urinary spot potassium (103 mEq/g creatinine). Complete blood count, liver function tests, renal function tests, random blood sugar, and stool examinations were all within normal limits. ABG analysis indicated the presence of both high anion gap and normal anion gap metabolic acidosis.

Radiological evaluation revealed cecal and sigmoid colonic thickening with inflammatory changes, along with bilateral mild pleural effusion and a thin rim of pericardial effusion. The further immunological assessment demonstrated a positive ANA profile with SSA/Ro60 (+4), SSA/Ro52 (+4), and SSB/La (+4) antibodies, indicative of pSS. Complement levels showed low C4 with normal C3, and rheumatoid factor (RA) was positive, whereas anti-cyclic citrullinated peptide (CCP) levels were within normal limits. Based on these findings, SS was considered the most likely diagnosis. Schirmer's test confirmed moderate ocular dryness.

The patient was treated with parenteral potassium and bicarbonate supplementation. Despite persistent hypokalemia, significant clinical improvement was noted following the initiation of low-dose corticosteroids. She was discharged on potassium and bicarbonate supplementation, along with low-dose corticosteroids, hydroxychloroquine, and thyroid hormone replacement. Follow-up evaluations showed continued improvement and a reduction in inflammatory changes.

CASE 3

A 35-year-old female presented with complaints of easy fatigability over the past 2 weeks, along with progressive weakness in all four limbs, difficulty in walking, and impaired ability to perform routine activities for the past 2 days. She had no significant past medical or drug history and no history of preceding fever, diarrhea, vomiting, or animal bites. There were no autonomic or sensory disturbances.

On examination, she was afebrile, hemodynamically stable, and fully conscious and oriented. There was no evidence of goiter, parotid, or lacrimal gland enlargement. Neurological evaluation revealed reduced muscle tone, muscle power of 3/5 in all four limbs, bilateral plantar flexor responses, and deep tendon reflexes of +1 in all limbs. Sensory examination was unremarkable, all cranial nerve functions were intact, and there were no speech disturbances or facial deviations.

Laboratory investigations showed significant hypokalemia (serum potassium: 1.5 mEq/L) with normal serum sodium levels (139 mEq/L). ABG analysis revealed normal anion gap metabolic acidosis with a urine pH of 7.2. Urinary electrolyte analysis demonstrated increased potassium loss (urinary potassium: 178 mEq/L; normal range: 22–164 mEq/L) and a urine anion gap of 20.6 mEq/L, suggestive of renal tubular acidosis. ECG revealed ST depressions with shallow and broad T waves.

Further immunological evaluation showed a positive ANA profile with SS-A and Ro52 antibodies. RA was markedly elevated (>100), whereas anti-CCP levels were within normal limits. Thyroid function tests revealed an elevated anti-TPO antibody level (624), with a significantly elevated TSH level (39) and normal free T3 and T4 levels. Although she did not report symptoms of dry mouth or facial swelling, these findings were highly suggestive of SS. Schirmer's test confirmed moderate ocular dryness.

The patient was initiated on parenteral and oral potassium supplementation along with bicarbonate replacement. Despite persistent hypokalemia, her condition improved significantly following the administration of low-dose corticosteroids. She demonstrated rapid clinical recovery, was able to walk the following day, and was subsequently discharged on oral potassium and bicarbonate supplementation. She was also started on low-dose corticosteroids, hydroxychloroquine, and thyroid hormone replacement therapy, with notable improvement observed during follow-up.

DISCUSSION

TIN is the most common renal manifestation of pSS. The term "autoimmune epithelitis" is often used to describe the damage caused by periepithelial accumulation of lymphocytes around the affected parenchymal epithelia. Studies have demonstrated a decreased activity of the H+-ATPase pump in the intercalated cells of the collecting ducts in SS, leading to impaired hydrogen ion (H+) excretion in the tubular lumen and subsequent metabolic acidosis.[5]

In the distal tubules, sodium ions (Na^+ are absorbed more rapidly than chloride ions (Cl^-), generating a "lumen-negative" transtubular gradient, which facilitates cation secretion. Since H^+ secretion is impaired, an increased amount of potassium ions (K^+) is excreted in the urine, resulting in hypokalemia. Hypokalemia leads to hyperpolarization of the resting membrane potential, making it more difficult to generate an action potential in muscle fibers, ultimately causing flaccid paralysis.

Citrate, a protective factor against renal stone formation due to its ability to chelate luminal calcium, is increasingly reabsorbed through the proximal tubule in acidemic conditions. Chronic acidemia promotes calcium phosphate release from bone stores, and the resulting high urinary pH favors the formation of calcium phosphate crystals, thereby predisposing patients to nephrolithiasis. Lifelong alkali replacement therapy at a dose of 1–2 mEq/kg is necessary to prevent acute hypokalemia as well as the long-term complications of osteomalacia and nephrolithiasis.

dRTA is characterized by normal anion-gap metabolic acidosis, a positive urine anion gap, alkaline urine, and hypokalemia. The most common electrolyte abnormality in dRTA is hypokalemia, which may result from decreased distal tubular sodium delivery, secondary hyperaldosteronism, defective H^+-K^+ATPase activity, or bicarbonaturia. Patients with SS and dRTA often exhibit interstitial nephritis with elevated levels of anti-carbonic anhydrase antibodies, which impair the function of carbonic anhydrase in the cortical collecting ducts.

Corticosteroids play a crucial role in managing pSS-related renal involvement. Studies have shown that corticosteroid therapy (0.5 mg/kg/day) alone can improve the estimated glomerular filtration rate in patients with pSS-associated interstitial nephritis. In our patient, potassium replacement therapy resulted in significant symptomatic improvement.[6-10] However, further research is necessary to elucidate the underlying disease mechanisms, and large-scale, multicenter, randomized controlled trials are warranted to evaluate the efficacy and safety of therapeutic agents such as corticosteroids and immunosuppressants in patients with various forms of renal involvement in pSS.

CONCLUSION

dRTA can present clinically with signs and symptoms of hypokalemia, such as muscular weakness, and is rare secondary to systemic diseases such as SS and SLE. Early diagnosis and prompt management of the underlying etiology are essential for improved outcomes. The primary treatment of dRTA involves supportive care, electrolyte replacement, and long-term monitoring to prevent complications.

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