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**Submission Category: Case Report**

**Title: A Case Report of Hypokalemic Periodic Paralysis Secondary to Sjögren's Syndrome with Distal Renal Tubular Acidosis**

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**Abstract**

We report a case of a 22-year-old female who presented sudden onset bilateral weakness of both upper and lower limbs. The patient had a history of hypokalemic periodic paralysis and dryness of the eyes. Laboratory investigations revealed metabolic acidosis and hypokalemia. Further investigations revealed distal renal tubular acidosis and positive anti-Ro and anti-La antibodies. Her potassium level was replaced and has been discharged with oral potassium supplements, steroids, and artificial tears

**Key clinical message:** Thiscase highlights the potential for an underlying autoimmune disease to be taken into account in a patient who presents with recurrent hypokalemic periodic paralysis secondary to distal renal tubular acidosis (RTA). Distal RTA is commonly associated with autoimmune disorders, thus identifying and treating the underlying condition is needed for better outcomes.

**Keywords:** Renal tubular acidosis, Sjogren’s syndrome, Hypokalaemia, periodic paralysis

**Introduction**

Sjögren’s syndrome (SS) is a rare autoimmune condition typically involving chronic inflammation of exocrine organs such as lacrimal and salivary glands, typically manifesting as dry eyes and mouth. However, extra-glandular renal involvement is not uncommon. This renal involvement can include the presence of anti-nuclear antibodies, glomerulonephritis, proteinuria, and/or tubulointerstitial nephritis, all of which can lead to severe kidney damage and even end-stage renal disease in some cases. In addition to the damage to the salivary glands and lacrimal glands, SS affects other exocrine glands and extracorporeal organs such as the kidneys and liver is frequently reported  [1] SS association with tubulointerstitial disease (e.g., tubulointerstitial nephritis, RTA, Fanconi syndrome, and glomerulonephritis) have been reported [2].  Renal involvement is well recognized extra glandular manifestation and occurs in 16% to 67% of primary Sjogren syndrome of which distal renal tubular acidosis (RTA) is common and reported in 4.3% to 9% of PSS patients. [3]

 Renal tubular acidosis (RTA) is characterized by renal tubular impairment in balancing physiologic acid bases. It often results from a defect in tubular transporters, which participate in the secretion or uptake of specific ions. This is due to congenital causes, exposure to nephrotoxic drugs, diuretic abuse, autoimmune disease, or malignancy. There are three major types of RTA: distal or type 1, proximal or type 2, and hyperkalemic or type 4. All three types of RTA are characterized by a positive urine anion gap, hyperchloremic non-anion gap metabolic acidosis, alkalotic or acidotic urine pH, and serum potassium derangements (hypo- or hyperkalemia). [4]

Because SS is insidious, the clinical manifestations are diverse making diagnosis difficult especially when it presents in an atypical manner. The clinical presentation is often nonspecific and the patient can have a wide range of symptoms that can mimic other conditions. Furthermore, the diagnosis of SS is complicated by the fact that the urine anion gap may not be elevated in every case, and the serum potassium levels may not be deranged. Therefore, it is important to consider other clinical findings in addition to laboratory tests when diagnosing SS.  We herein reported a case of type I RTA secondary to SS. As a result of this case report, we can gain a better understanding of renal involvement in patients with Sjogren's disease. It is important to identify Sjogren's syndrome early and begin treatment, to reduce the risk of severe and possibly fatal complications. Additionally, clinicians should be aware of the potential renal involvement in these patients to provide timely and effective treatment. This case report provides evidence of the potential for renal tubular acidosis to occur in Sjogren's syndrome patients. The report also outlines the importance of early detection and timely treatment of hypokalemic periodic paralysis, as this can greatly reduce the risk of fatal recurrences. This information may help clinicians identify and treat Sjogren's syndrome patients with renal involvement more effectively, and help improve the outcomes of these patients.

**Case report**

A 24-year-old female patient presented to ER department of a tertiary care hospital with complaints of acute onset of muscle weakness in bilateral upper and lower limbs for one day. The weakness was painless, and not associated with loss of consciousness. She didn’t have any preceding respiratory or gastrointestinal problems. There was no history of steroid use or laxative abuse. The weakness was prominent in both the proximal and distal extremities. On further inquiry, the patient had dryness in the eyes. She didn’t have any rash or joint pain or alopecia. The patient had a history of admission to the medical unit for the same problem. The laboratory evaluation at that time revealed hypokalemia which was treated with KCL infusion. Family history was not significant for similar conditions. On examination, she was normotensive with a blood pressure of 120/70, a pulse of 77 bpm, a temperature of 98 °F, and spo2 of 99%. Thyroid was normal on examination. She had no muscle tenderness, reflexes were 2/2, power was 3/5 in both upper and lower limbs, time was 2/3, GCS was 15/15, and planters were down bilaterally.

On investigation, she had hypokalemia and further lab workup revealed a normal anion gap metabolic acidosis as shown in (Table.1).

**Table.1** Lab investigations

|  |  |  |
| --- | --- | --- |
| **Laboratories** | **Values** | **Reference ranges** |
| Hemoglobin | 12.8 | 12.1 - 15.1 g/dL |
| WBC | 9.05 | 4.5 - 11.0 × 109/L |
| Platelet | 255 | 150 - 400 × 109/L |
| Sodium | 138.7 | 135.0–150.0 mmol/L |
| Potassium | **2.52** | 3.5–5.1 mmol/L |
| Chloride | **115** | 96.0–112.0 mmol/L |
| Glucose | 76.8 | 70-1140 mg/dL |
| Magnesium | 2.4 | 1.5- 2.5 mg/dL |
| Calcium | 9.26 | 8-10  mg/dL |
| Total bilirubin | 0.55 | 0.1 -1.0 mg/dL |
| ALT/GPT | **86.1** | 10-50 U/L |
| Alkaline phosphatase | **132** | 35- 104 U/L |
| Creatinine | 0.86 | 0.42- 1.06 mg/dL |
| PTH | 8.88 | 7 -53 pg/mL |
| TSH | 2.15 | 0.3- 4.2 mg/dL |
| Free T3 | 1.16 | 0.6-2.0 nmol/L |
| Free T4 | 15.04 | 10-28 pmol/L |
| HIV | Negative | - |
| HBsAg | Negative |  |
| HCV | Negative | - |

WBC: white blood cells; ALT/GPT: Alanine aminotransferase/ Glutamic-Pyruvic Transaminase; PTH: Parathormone; TSH: thyroid stimulating hormone; HIV: human immunodeficiency virus; HBsAg: Hepatitis B surface antigen; hepatitis C virus; mmol/L: millimole per liter; mg/dL: milligram per deciliter; U/L: units per liter; pg/dL: picogram/deciliter; nmol/L nanimil/liter; pmol/L: picomoles per liter.

Arterial blood gasses of the patient were sent and showed normal anion gap metabolic acidosis with a PH of 7.21, bicarbonate of 16 mEq, and partial pressure of carbon dioxide (pCo2) of 36.5 mm Hg. The patient’s serum electrolytes and arterial blood gasses revealed hyperchloremic normal anion gap metabolic acidosis and a suspicion of distal RTA was made which was confirmed by urinary electrolytes and urinary PH. The patient urinary electrolytes revealed a positive anion gap as shown in (Table.2).

Table.2. Urinary electrolytes and anion gap.

|  |  |  |
| --- | --- | --- |
| **Urine electrolytes** | Value | Range |
| pH- urine | 7.0 | 4.5–7.8 |
| Sodium | 23 mEq/L | 40-220 mEq/L |
| Potassium | 21.7 mEq/L | 25-125 mEq/L |
| Chloride | 26 mEq/L | 110-250 mEq/L |
| Anion gap | 18.7 mEq/L | 3-16 mEq/L |

As a result of the patient's dry eyes, it was speculated that Sjogren's syndrome was associated with distal RTA. In the shimmer test, the score was less than 5 mm in 5 minutes, indicative of tear deficiency. An autoimmunity profile was reported positive for anti-Sm/RNP antibodies, anti-SSA/Ro antibodies, and anti-SSB/La antibodies. The patient was diagnosed with a case of primary Sjögren's syndrome that leads to distal RTA and presents as recurrent hypokalemic periodic paralysis based on American College of Rheumatology/European League Against Rheumatism (ACR‐EULAR) classification criteria for primary Sjögren's syndrome in which the patient scored 4 out of 9.

Patients were treated with intravenous potassium, oral potassium supplements, prednisolone of 1 mg/kg, and omeprazole 40 mg once daily, along with artificial tears. Follow-up was requested at 4, 8, and 16 weeks. After four weeks of follow-up, the patient's potassium level remained stable at 4.0 mEq, and the oral prednisone was tapered at eight weeks. Three months have passed since she last had symptoms.

**Discussion**

Sjogren's syndrome is a multi systemic autoimmune disorder commonly presented as lacrimal and salivary gland dysfunction. Renal involvement in pSS has a prevalence of around 9%, although the first clinical manifestation with renal involvement is uncommon. Renal involvement in pSS is either due to tubule interstitial involvement or less commonly glomerular involvement. Lymphocytic infiltration of the kidney tubules by T cells, B cells, or plasma cells has been hypothesized as behind the pathogenesis of renal involvement. Other causes include decreased hydrogen ion secretion secondary to the absence of a vacuolar H+ ATPase pump in the distal tubules and antibodies to the thiazide-sensitive NaCl co transporter (NCCT). The presence of anti-SSA, anti-SSB, and hypergamma globulinemia are the only risk factors predisposing to renal involvement in pSS. This autoimmune condition typically involves lymphocytic infiltration of the salivary, parotid, and lacrimal glands. This results in xerosis (dry eyes) and xerostomia (dry mouth). However, Sjögren’s syndrome is often characterized by SICA symptoms, but they are not always present. [5]

In most cases, it affects the renal tubules through TIN and occasionally through autoantibodies. All segments of the nephron can be involved in pSS. This leads to distal and proximal RTA, Fanconi syndrome, diabetes insipidus, and less commonly Gitelman's syndrome and Bartter's syndrome. Of these, distal RTA is the most frequent tubular dysfunction in pSS. Hypokalemia and metabolic acidosis in distal RTA causes muscle weakness and periodic paralysis. Clinical features include mild hypokalemia, diabetes insipidus, renal tubular acidosis, profound hypokalemic periodic paralysis, and Fanconi syndrome [6]. Glomerular involvement manifesting as proteinuria, haematuria, and severe renal dysfunction is uncommon. Renal tubular acidosis with severe hypokalemia causing paralysis is the most common manifestation of renal involvement in Sjogren's syndrome, although it is underdiagnosed.  [6, 7]

In both primary and secondary Sjögren syndrome, dRTA seems to be more prevalent in autoimmune diseases. Other autoimmune diseases such as systemic lupus erythematosus (SLE), primary biliary cirrhosis (PBC), autoimmune hepatitis (AIH), and Rheumatoid Arthritis are less commonly associated with dRTA. [8] The association of dRTA with autoimmune diseases is listed in (Table.3).

**Table.3:** Association of distal RTA with autoimmune diseases

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **patient** | **Age** | **Diagnosis** | **Presentation** | **Blood pH** | **Urine pH** | **Lab findings** | **Treatment** | **Outcome** | |
| Abdulla et al.–(2017)  [9] | Female | 57 | Sjögren syndrome | SICCA, Fracture, hypocalcemia, anemia (9.8 g/dL) | Ns | 6.5 | Serum K= 2.3 mmol/L HCO3= 13 mmol/L  Creatinine= 1.1 mg/dl | K+, HCO3-, supplements HCQ | K+ correction | |
| Ammad Ud Din et al.–(2020)  [10] | Female | 44 | SLE | Hypokalemic paralysis, SICCA, proteinuria | 7.21 | 6.5 | Serum K= 1.6 mmol/L HCO3= 10 mmol/L  Creatinine= 0.8 mg/dl | K+, HCO3− supplements; Prednisone 20 →40 mg/day, HCQ | | K+ correction, proteinuria remission |
| Elitok et al.–  (2020)  [11] | Female | 60 | Primary biliary cirrhosis | Progressive chronic kidney disease, leukocyturia | 7.23 | 7 | Serum K= 3.3 mmol/L HCO3= 11.1 mmol/L  Creatinine= 1.93 mg/dl | Not specified | | Not specified |
| Duarte Silveira et al.–  (2022)  [12] | Female | 67 | Rheumatoid arthritis | Peripheral arterial disease, hypomagnesemia | 7.38 | 6.5 | Serum K= 3.1 mmol/L HCO3= 15.7 mmol/L  Creatinine= 0.51 mg/dl | K+ supplements | | Not specified |

The latest and new American College of Rheumatology/European League Against Rheumatism (ACR‐EULAR) classification criteria for primary Sjögren's syndrome are the result of international collaboration and have been derived using a well‐established and validated methodology. According to Table 3.3, the classification of primary Sjögren's syndrome is assigned to anyone who meets the inclusion criteria and scores four out of five when the weights from the 5 criteria in the table are combined. A score of 4 was achieved after positive results from the AntiSSA and antiRo tests, along with Schirmer's test. A positive Anti-SSA/anti-Ro antibody, a positive Schirmer's test, dry eyes, and mouth, as well as a positive minor salivary gland biopsy, are all criteria in Table 3. All five criteria of primary Sjögren's Syndrome were met in the patient, so the weights from each criterion were added up to give the patient a score of 4.

**Table .3** American College of Rheumatology/European League Against Rheumatism (ACR‐EULAR) classification criteria for primary Sjögren's syndrome

|  |  |
| --- | --- |
| **Items** | **Weight/Score** |
| Labial salivary gland with focal lymphocytic sialadenitis and focus score of ≥1 foci/4 mm2 | 3 |
| Anti‐SSA/anti‐Ro positive | 3 |
| Ocular staining score ≥5 (or van Bijsterveld score ≥ 4) in at least one eye | 1 |
| Schirmer's test ≤5 mm/5 min in at least one eye | 1 |
| Unstimulated whole saliva flow rate ≤0.1 ml min−1 | 1 |

Treatment of Sjogren’s syndrome depends on initial symptoms and extra glandular manifestations. Severe and acute systemic manifestations require the treatment of corticosteroids with or without immunosuppressive agents. Management of dRTA is essentially supportive, including potassium and bicarbonate supplementation and nephron-urological follow-up to prevent complications from nephrolithiasis. Corticosteroids are used to reduce inflammation and modulate the immune response, while immunosuppressive agents help to further reduce the activity of the immune system. Potassium and bicarbonate supplementation helps to maintain electrolyte balance and prevent the development of nephrolithiasis, which can cause further complications. 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. [14] Our patient responded well to treatment with prednisone. By supplementing potassium and bicarbonate, the kidneys can maintain the electrolyte balance, which prevents the formation of nephrolithiasis. Additionally, prednisone helps to reduce symptoms associated with the condition, such as inflammation and swelling and improves the patient's overall well-being. As curative treatments remain to be elucidated, monitoring for complications such as nephrocalcinosis, nephrolithiasis, and rickets/osteomalacia should also take place along with ongoing treatment of metabolic derangements and symptoms. [15]

**Conclusion**

Sjogren's disease and hypokalemic periodic paralysis are rare combinations. Hypokalemic periodic paralysis associated with metabolic acidosis must be taken into consideration when analyzing Sjogren's syndrome. Prompt diagnosis and appropriate management of the condition can improve the patient's prognosis. Detecting hypokalemic periodic paralysis associated with renal tubular acidosis in its earliest stages and treating it promptly can prevent the potentially fatal recurrence of such episodes.

**Ethical Approval**

Not required

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**Consent**

Written informed consent was obtained from the patient to publish this case report. Consent can be provided upon the Editors in chief request.

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**Declaration of competing interest**

The authors declare no conflict of interest.

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