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RARE CASE REPORT

Hypokalemic periodic paralysis due to distal renal tubular acidosis as the initial presentation of Sjögren's syndrome.

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Abstract

Sjögren's syndrome is an autoimmune disease characterized by lymphocytic infiltration of the exocrine glands resulting in xerostomia, dry eyes (keratoconjunctivitis sicca), and profound B-cell hyperactivity. Middle-aged women are primarily affected with female: male ratio 10-20:1, although Sjögren's syndrome may occur at any age, including childhood. In this case report, we discuss a case of a 30 years female with distal renal tubular acidosis (RTA), who had experienced severe hypokalemic episodes since the age of 25 years; the patient was eventually diagnosed with Sjögren's syndrome. She was managed with potassium and alkali repletion therapy.

Introduction

Renal tubular acidosis (RTA) is characterized by renal tubular impairment in maintaining physiological acid-base balance. It mostly results from a defect in tubular transporters, which participate in the secretion or uptake of specific ions, or due to congenital causes, exposure to nephrotoxic drugs, diuretic abuse, autoimmune disease, or malignancy (e.g., multiple myeloma). There are three types of RTA: distal or type 1 or classic RTA, proximal or type 2, and hyperkalemic or type 4. All three types of RTA are characterized by hyperchloremic non-anion gap metabolic acidosis, alkalotic or acidotic urine pH, positive urine anion gap, and serum potassium derangement (hypo- or hyperkalemia).

Distal RTA can be caused by either impaired H+ secretion (secretory defect) or an abnormally permeable distal tubule, resulting in increased backleak of normally secreted H+ (gradient defect); it may be genetic or acquired. Medicines like amphotericin, result in increased backleak of protons across the apical plasma membrane, leading to a gradient defect form of distal RTA. It can be further defined by urinary pH (>5.5) and profound hypokalemia (<3 mmol/L). Consequently, due to an impaired luminal gradient, ionic wasting occurs, leading to the possible development of nephrocalcinosis, nephrolithiasis, rickets/osteomalacia, muscle weakness, and respiratory failure. Distal RTA can be a rare complication of Sjögren's syndrome in adolescents. In this report, we discuss a case of

distal RTA secondary to Sjögren's syndrome in a middle-aged woman leading to hypokalemia and hypokalemic periodic paralysis and her management with potassium and alkali repletion.

Case Presentation

A 30 years female with five years history of multiple hospitalizations for hypokalemic paralysis was brought to the emergency room for sudden-onset bilateral lower limb weakness progressing to the shoulder and biceps after awakening from a nap. The patient reported that these symptoms were similar to the episodes in past. System review did not reveal abdominal pain, emesis, diarrhea, painful swollen stiff joints, band-like sensation, or the use of non-steroidal anti-inflammatories (NSAIDs). There was no personal or family history suggestive of autoimmune diseases. She was vitally stable and no abnormal finding was identified on physical examination. Initial lab investigations revealed sodium 138 mmol/L, potassium 2.2 mmol/L, chloride 116 mmol/L, and bicarbonate 16 mmol/L. The pH of venous gas was 7.19 (normal anion gap acidosis). Urine sodium was 57 mmol/L, urine potassium 40 mmol/L, and urine chloride 51 mmol/L (+ve urine anion gap: 46 mmol/L), and urinary pH was 6.5 without blood or protein.

Laboratories	Values	Reference range
Serum Chemistry		
Sodium	138	135-145 mmol/L
Potassium	2.2	3.5-5.0 mmol/L
Chloride	116	95-105 mmol/L
Bicarbonate	16	12-22 mmol/L
Urine Chemistry		
Urinary pH	6.5	4.5-7.8
Sodium	57	40-220 mmol/L
Potassium	40	25-125 mmol/L
Chloride	51	14-50 mmol/L
Anion gap	46	<10 mEq/L
Venous blood gas		
Ph	7.19	7.31-7.45
Autoimmune Panel		
ANA	1:640(speckled)	<1:80
Anti-dsDna	Negative	<20 AU/ml
Anti-Smith	Negative	0-40 AU/ml
Anti-RO/SSA 52	260	0-40 AU/ml
Anti-LA/SSB	140	0-40 AU/ml
Anti-U1RNP	Negative	0-40 AU/ml

Without a history of gastrointestinal losses or administration of intravenous fluids, and the presence of metabolic acidosis along with a positive urinary anion gap and a urine pH of 6.5, she was diagnosed as a case of distal (type I) RTA. She was promptly hydrated with intravenous normal saline and was given potassium chloride and sodium bicarbonate, which corrected both her hypokalemia and hyperchloremic non-anion gap metabolic acidosis. She was later discharged on oral potassium chloride and sodium bicarbonate. Over the next few months, the patient had several similar presentations at hospitals for upper and lower extremity weakness and paralysis secondary to hypokalemia. Initially, suspicion of disordered eating/exercise or diuretic/laxative abuse as a contributor to her metabolic derangements was low based on the patient report and chart review. On further probing, she admitted to infrequent, intermittent dry mouth and dry eyes with a sand-like sensation associated with ocular pruritus for several months, but denied any history of eye inflammation, use of artificial teardrops, or increased occurrence of cavities. Ophthalmology consultation was done for Schirmer's test and it was positive (<5mm/5 minute on right eye). Her autoimmune panel was positive for antinuclear antibodies (ANA) (1:640) and anti-Ro/SSA antibody (SSA-52: 260 AU/mL and SSB:140 AU/mL) and negative for anti-double-stranded DNA (dsDNA), anti-Smith, and anti-U1-ribonucleoprotein (RNP) antibodies. (Table1). Diagnostic tests for SCN4A deletion/duplication, hepatitis C, and HIV were negative. Given the patient did not have other derangements of urine and serum electrolytes, other causes of renal tubulopathies, such as Barter, Gitelman, and Fanconi syndromes were subsequently ruled out. Based on sicca symptoms, positive Schrimer's test, and positive anti-Ro/SSA anti-La/SSB antibodies, a presumptive diagnosis of Sjögren's syndrome was made.

Differential diagnosis

There are many causes of RTA, the most common of which are autoimmune disorders (Sjögren's syndrome, systemic lupus erythematosus (SLE), and rheumatoid arthritis), medications (ifosfamide, amphotericin, and ibuprofen), hyperparathyroidism, vitamin D intoxication, sarcoidosis and Wilson's disease.

Treatment

Patients with renal tubular acidosis should receive sodium bicarbonate orally (0.5–2 mmol/kg in four divided doses). Glucocorticoids and antibodies to CD20 (rituximab) have a role in patients with systemic disease, particularly in those with purpura and arthritis. Hydroxychloroquine (HCQ) appears to be effective in arthritis. This patient was treated with pilocarpine 5mg 1 tablet PO QID. Syrup, potassium citrate 15ml with water QID, and artificial tears for eyes.

Outcome and follow-up

Her symptoms of dry eye and dry mouth improved and she had not developed paralysis since then.

Discussion

Sjögren's syndrome is an autoimmune exocrinopathy characterized by lymphocytic infiltration of the exocrine glands (primarily salivary and lachrymal glands) and hyperreactivity of B lymphocytes. The latter is manifested by hypergammaglobulinemia and the presence of serum autoantibodies against non-organ-specific antigens like immunoglobulins (rheumatoid factors) and extractable cellular antigens (Ro52, Ro60, and La). This immune process can even affect non-exocrine organs, like the skin, gastrointestinal tract (GIT), kidneys, and lungs. Although sicca symptoms are a characteristic symptom of Sjögren's syndrome, they are not always present. A case series by Shioji *et al* (1) revealed four cases of Sjögren's syndrome complicated by RTA, within which three of the four patients presented with arthralgia or muscle weakness. Only two reported dryness of the mouth and none reported any ocular abnormality. Several case reports have also reported muscle weakness (2), pathological fractures (3), and hypokalaemic paralysis (4) as the presenting symptoms of Sjögren's syndrome secondary to distal RTA. Therefore, the symptoms associated with RTA, even in the absence of sicca symptoms, maybe a clue that triggers the discovery of Sjögren's syndrome. There are two types of the disease: Primary and secondary Sjögren's syndrome. Primary Sjögren's syndrome is thought to be an isolated condition infrequently caused by another pathological process, whereas secondary Sjögren's syndrome is the sequelae of other rheumatological diseases like systemic lupus erythematosus, rheumatoid arthritis, and scleroderma. Sjögren's syndrome often affects middle-aged females, with a sex-adjusted prevalence of 2.2-10.3 per 10,000 individuals (5). It is often diagnosed based on the American-European Consensus Group's (AECG) criteria for Sjögren's syndrome. Recurrent parotid swelling is the most common presenting symptom in the pediatric age group, occurring more frequently than sicca symptoms (6). The most common renal manifestation of Sjögren's syndrome is tubulointerstitial nephritis, which may present as RTA in adult populations; however, RTA is rare in the pediatric population as it accounts for 7.1-19.2% of cases who present with renal potassium wasting or hypokalemic paralysis (7). Our patient first presented with an episode of muscle weakness in form of paraparesis and ascending upward in the setting of severe hypokalemia at the age of 25 years, often exacerbated by menses. Study by Sandhya et al.,revealed that adequate levels of estrogen and androgens were related to increased protection of glandular epithelial cells from apoptosis and lymphocytic infiltration (8). Therefore, the mechanism whereby decreased levels of sex hormones result in lymphocytic tubulopathy may explain the association with the patient's hypokalemic exacerbation during menses. Over five years, our patient was hospitalized for several episodes of symptoms associated with severe hypokalemia secondary to distal RTA. With every hospitalization, the chance to make the diagnosis of Sjögren's syndrome was missed, probably because of a lower index of suspicion based on age and the absence of classical signs and symptoms at the time. Autoimmune antibodies for Sjögren's syndrome demonstrated high serum ANA and anti-Ro/SSA-52 and -60, suggesting a higher suspicion for the disease, especially as SSA-52 has a prevalence rate of 63.2% in Sjögren's syndrome (9). The presence of high anti-Ro/SSA titers has also been related to a greater likelihood of earlier disease onset and extra-glandular involvement (10,11,12)

Conclusion

The early diagnosis of Sjögren's syndrome is difficult as current diagnostic guidelines contribute to a higher likelihood of missed diagnosis, and these patients may present with heterogeneous findings inconsistent with the classical presentation of the disease. Thus, adolescent patients presenting with evidence of renal pathology should undergo further diagnostic evaluation to rule out Sjögren's syndrome while simultaneously receiving prompt management of metabolic derangements with potassium and alkali treatment to prevent potentially fatal sequelae.

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