case report

Primary Sjögren's syndrome presenting as hypokalemic paralysis

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Sjögren's syndrome (SS) is a chronic inflammatory disorder that usually presents with dry mouth (xerostomia) and dry eyes (xerophtalmia or keratoconjuctivitis sicca) and is frequently associated with arthralgia or a connective tissue disorder.[1] SS can be seen alone (primary) or in association with other autoimmune rheumatic disease (secondary). Thus, the diagnostic approach to SS is rather complicated because it must include two different goals: assessment of the ocular and salivary components, and differentiation between the primary and secondary variants of the syndrome. Most of the rheumatic diseases lack a single distinguishing feature, but each disease is usually identified by the presence of a combination of clinical and laboratory manifestations. In practice, the clinical observation by an expert clinician may be considered as the only available "gold standard" for determination of a diagnosis, but for the correct classification of patients with primary and secondary SS the revised international classification criteria for SS should be used.[1]

Renal abnormalities in SS include diminished ability to concentrate urine in about half of all cases, distal renal tubular acidosis in 15%, nephrocalcinosis and less often, interstitial nephritis and glomerular diseases.[2,3] Although hypokalemia in patients with SS is a frequent sequelae of renal tubular acidosis, a severe symptomatic decrease in serum potassium concentration has been described in a few cases only. In this case report, we describe a case of a patient with Sjögren's syndrome in whom the first manifestation of disease was paralysis due to hypokalemia and distal tubular acidosis. This type of presentation is rare since only a few cases have been reported in the literature.[4,5]

CASE REPORT

A 31-year old Caucasian woman from Croatia was admitted to our hospital due to progressive muscular weakness and myalgia that began in her extremities 2 days previously. She had been healthy and denied any other symptoms such as arthralgia, fever, skin rush and diarrhea, and she did not take any medication. However, she described a continuous sensation of dryness of her eyes and mouth. On examination, blood pressure was 110/70 mm Hg, heart rate 77/minute, temperature 36.5° C, and respirations 26/min. She had flaccid paralysis of her arms and legs with diminished tendon reflexes. She was unable to move her extremities. The neurological assessment of the patien (according to the Medical Research Council of Great Britain) showed that peripheral sensation was intact and no abnormalities of the cranial nerves were detected. The rest of the physical examination was unremarkable. Results of laboratory investigations at the time of admission are shown in Table 1.

An initial diagnosis of hypokalemic periodic paralysis and a non-anion gap acidosis was made. Moreover, severe hypokalemia with increased urine pH was also present. The urine anion gap was positive (54 mmol/L), despite a high urine chlorine concentration. The patient was started with intravenous administration of potassium and bicarbonate. Administration of potassium and sodium bicarbonate corrected hypokalemia and metabolic acidosis leading to the recovery of her motor function, but the alkaline urine pH was not corrected. The presence of a high urinary pH despite hyperchloremic acidosis was consistent with distal renal tubular acidosis (RTA). To confirm the diagnosis of distal RTA we performed two more tests: the ammonium chloride loading test and fractional excretion of bicarbonate test. The administration of ammonium chloride (0.1g/kg) caused metabolic acidosis, but did not increase the urinary excretion of ammonium and titratable acid, and did not lower urinary pH below 7. The results of the fractional excretion of bicarbonate (1.6%) indicated distal tubular acidosis. The presence of unexplained renal tubular acidosis as well as the elevated serum total

Table 1. Laboratory parameters of the patient.

Parameter	
Arterial pH	7.21
Arterial pCO2 (mmol/L)	3.7
Serum bicarbonate (mmol/L)	14
Serum potassium (mmol/L)	2.10
Serum sodium (mmol/L)	135
Serum chlorine (mmol/L)	110
Serum anion gap (mmol/L)	11
Serum creatinine (µmol/L)	77
Serum osmolality (mOsmol/L)	289
Serum total proteins g/L	83
Urine sodium (mmol/L)	165
Urine potassium	54
Urine chlorine (mmol/L)	162
Urine anion gap (mmol/L)	57
Urine pH	8.0
Urine osmolality (mOsmol/L)	261

protein concentration and dryness of eyes led us to investigate for the presence of Sjögren's syndrome.

Schirmer's test demonstrated 5 mm of tear flow at 5 minutes. Biopsy of the minor salivary glands of the lip showed lymphocytic infiltration and epimyoepithelial islands of ectasia in the ducts, indicating Sjögren's syndrome. Serologic tests revealed increased rheumatoid factor, 250 IU/mL (normal range, 0-40 IU/mL), positive antinuclear antibodies and positive antibodies for SS-A (Ro) >160 U/mL (normal range, 10-15 U/mL). No antibodies for DNA and SS-B (La) were detected. HLA analysis showed HLA-A 1 and 2, HLA-B 8 and 27, HLA-DR 2 and 11.Further immunological investigation revealed polyclonal hyperglobulinemia without monoclonal paraproteins, IgG 24.75 g/L (normal range, 7-16 g/L), IgA 4.16 g/L (normal range, 0.7-4.0 g/L), IgM 1.78 (normal range, 0.4-2.3 g/L). Thyroid function tests were within normal ranges. Ultrasonographic examination of the kidneys and creatinine clearance were normal. The discharge diagnosis was Sjögren's syndrome and distal renal tubular acidosis causing hypokalemic paralysis. The patient was discharged with a prescription of oral potassium and sodium bicarbonate. One month after discharge the laboratory findings were good (serum potassium 4.4 mmol/L, bicarbonate 23 mmol/L and arterial pH 7.36).

DISCUSSION

Our patient fulfilled all criteria for the diagnosis of Sjögren's syndrome.[1] Hypokalemic paralysis was the presenting manifestation of primary Sjögren's syndrome in this patient on admission at the Emergency Department. Renal involvement has been estimated to occur in 30% to 40% of Sjögren's syndrome.[6] Patients with Sjögren's syndrome may have clinical and pathological evidence of both proximal and distal types of renal tubular acidosis.[6] Our patient exhibited distal renal acidosis. Hypokalemia commonly accompanies renal tubular acidosis, but severe symptomatic hypokalemia is rare.[7,8] After the medical history was recorded again, data about xerostomia and xerophtalmia were noticed. Thus, the symptoms of xerostomia and xerophtalmia should prompt screening for underlying systemic autoimmune diseases, especially Sjögren's syndrome. Upon admission of this patient, metabolic acidosis associated with hypokalemia and inappropriate high urine pH suggested a distal renal tubular acidosis, which was subsequently confirmed by studies of the ammonium renal acidification test and fractional excretion of bicarbonate. In healthy people, the urinary anion gap has a negative value, since the chloride concentration exceeds that of sodium plus potassium. The finding of a positive urinary anion gap during acidosis (an indirect measure for reduced ammonium excretion) is very reliable for confirmation of the diagnosis of distal renal tubular acidosis caused by decreased ammonium ion excretion.[9] Hypokalemia is also associated with metabolic acidosis in proximal tubular renal acidosis, which is characterized by high-grade urinary bicarbonate wasting, but in our patient fractional excretion of bicarbonate was low, which was diagnostic for distal tubular renal acidosis. Fractional excretion of bicarbonate in proximal renal tubular acidosis is greater than 15% to 20%.

The pathogenesis of renal involvement with Sjögren's syndrome remains obscure, although the secretory defect in distal tubules due to an immunologic mechanism is suspected. Current postulation for distal RTA is inhibition of hydrogen-potassium adenosine triphosphatase in renal principal cells and H intercalated cells.[10] The histological lesion in the kidney of patients with Sjögren's syndrome and renal tubular acidosis is characterized by a prominent interstitial infiltrate composed of lymphocytes and plasma cells with secondary invasion of the tubular membrane and limiting epithelium.[2,3,11] It has been postulated that this inflammatory process disrupts the cellular architecture, resulting in defective hydrogen ion secretion, and in fact, the absence of intact hydrogen ATP-ase in the intercalated cells of renal biopsy specimens has been shown by immunohistochemistry

in patients with Sjögren's syndrome and distal renal tubular acidosis. The histological lesions in the kidney in patients with Sjögren's syndrome are not specific because similar lesions can be found in other pathologic conditions (e.g., interstitial nephritis caused by drugs, immunological diseases of the kidney).[2,3] In our patient the kidney biopsy was not performed, because other tests were sufficient for the diagnosis of distal renal tubular acidosis and Sjögren's syndrome. The peritubular infiltrates in the kidney may be considered the analogue of the periductal infiltrates in the salivary glands.[2] The salivary gland infiltrates synthesize excessive quantities of immunoglobulin and the kidney contains cells making immunoglobulin.

In conclusion, hypokalemic paralysis as the initial manifestation of primary Sjögren's syndrome is rare. When it occurs it may precede symptoms of xerostomia and xerophtalmia. Thus, the diagnosis of primary Sjögren's syndrome should be considered in young woman who present with rapidly progressive weakness and hypokalemia,[4,12,13] with or without the sicca complex. This case demonstrates that primary Sjögren's syndrome can be revealed by life-threatening signs of hypokalemia due to renal tubular involvement.

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