CASE REPORT

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Hypokalaemic Periodic Paralysis with Renal Tubular Acidosis in Patients with Primary Sjögren's Syndrome Presenting as Quadriparesis and Recurrent Paraparesis

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Introduction

Sjögren's syndrome is a slow-progressing autoimmune disorder that involves exocrine glands, mostly lacrimal and salivary glands, resulting in impaired secretion of these glands, termed as sicca symptoms which is a combination of dry eyes (keratoconjuctivitis) and dry mouth (xerostomia)[1]. In addition to salivary glands and lacrimal glands involvement, Sjögren's syndrome affects other exocrine glands and organs such as the kidneys and liver. Primary Sjögren's syndrome commonly involves kidneys leading to Tubulointerstitial nephritis, type 1 Renal Tubular Acidosis (RTA), Fanconi syndrome, and Glomerulonephritis. Renal involvement is seen in 16% to 30% of patient. Type 1 or distal Renal Tubular Acidosis (RTA) is the most common presentation. Sjögren's syndrome is more commonly seen in middle-aged women with a female to male preponderance ratio of 9:1[2]. Hypokalaemic paralysis is the initial symptom in only 7% of patients with Sjögren's syndrome[2]. A diagnosis of hypokalaemic paralysis should be considered in a patient with hypokalaemia who presents with quick-onset neurological symptoms[3].

We hereby present two cases of hypokalaemic periodic paralysis presenting as quadriparesis and paraparesis, with distal renal tubular acidosis, which were later diagnosed to be secondary to Sjögren's syndrome. Informed consent was taken from each of these patients to present these as case reports.

Case report 1

A 35-year-old female presented to the medicine OPD with a 3-days history of sudden onset bilateral lower limb weakness involving proximal and distal muscles, swelling, and tingling sensation in bilateral lower limbs. Patient had mild dyspnoea, fever with chills and rigors, dry cough, history of dryness of mouth and foreign body sensation in eyes since 1 year. She had no history of altered sensorium, seizures, and vomiting, gastrointestinal symptoms like diarrhoea, joint pain, rashes and alopecia, use of steroids or laxative abuse, or herbal medicines in the past. She had no history of diabetes, hypertension, asthma, or tuberculosis. She did not have bladder or bowel involvement. She had three episodes of sudden-onset bilateral lower limb weakness, around one month back, around one year back, and around one- and half-years back; all improved with treatment.

On physical examination, patient was well-oriented to time, place, and person; the cranial nerves examination was normal; all deep tendon reflexes were diminished; the muscle power of both lower limbs was 1/5 and the upper limbs was 5/5 by Lovett's scale; and the rest of the CNS examination was normal. Other organ examinations, like gastrointestinal, respiratory, and cardiovascular, were normal. Her tongue was dry, and infralingual salivary pooling was present. Her vital signs on admission were temperature 98.9° F, heart rate 90 beats per minute, respiratory rate 20 breaths per minute, oxygen saturation 97% at room air, capillary blood glucose 110 mg/dL, and blood pressure was 106/70 mmHg. Routine investigations were sent, which are mentioned in Table I below. Serum potassium level was 2.1 mEq/L, and ABG revealed normal anion gap metabolic acidosis with urinary pH of 5.7. As her history of dryness in the mouth pointed towards an autoimmune disorder, an anti-nuclear antibody by Immunofluorescent technique (ANA by IFA) was sent, which came positive in a 1:80 titre with speckled pattern grade one+, ANA profile was sent to confirm, which revealed positive SS-A and SS-B antibodies, which are positive in Sjögren's syndrome. An ophthalmologist's opinion was taken to further investigate Sjögren's syndrome. Schirmer's test was conclusive in favour of Sjögren's syndrome, her left eyes showed no signs of tears, (i.e., a very severe form of dry eye), and the right

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eye revealed moderate dry eye (6 mm). Her TFBT (Tear Film Break-Up Test) revealed dryness in both eyes; all were conclusive in favour of Sjögren's syndrome. With the help of history, examination and lab results, diagnosis of distal RTA (dRTA) with primary Sjögren's syndrome causing hypokalaemic periodic paralysis was made. For hypokalaemia, the patient was treated with intravenous potassium chloride and sodium bicarbonate. Further, hydroxychloroquine was started with a dose of 200 mg once daily, and steroids with a dose of 1 mg/kg body weight were initiated. The patient responded to the treatment, and her clinical profile showed improvement. The patient was discharged as her symptoms improved. The patient has been on regular follow-up for the last 5 months, is asymptomatic, and is on a tapering dose of steroids and alkali supplements.

Case report 2

A 23-year-old female student, a known case of hypothyroidism, resident of Bikaner, Rajasthan, developed sudden onset weakness in all four limbs while she was walking towards her house. She fell down and was taken to a nearby hospital where basic investigations were done. The weakness was symmetrical and non-progressive in nature. Arterial blood gas analysis was suggestive of severe metabolic acidosis with hypokalaemia (S. potassium: 1.5 mEq/L). Supportive treatment was given, and she was referred to a higher centre. On the way in the ambulance, she had an episode of asystole, for which she received cardiopulmonary resuscitation (CPR). The return of spontaneous circulation was achieved. She was intubated for better resuscitation efforts and brought to our centre. The patient was immediately admitted to the ICU, and all baseline investigations were sent, which are mentioned in Table I.

Intravenous potassium with magnesium were started, along with supportive treatment. The patient was intubated and was on FiO_2 40%. She had deranged sensorium so MRI of the brain was done. It was suggestive of hypoxic ischaemic encephalopathy. Besides this, the patient had recurrent hypokalaemia. Even after correction, potassium levels were below normal levels. There was no plausible cause for recurrent hypokalaemia. Distal RTA was kept as a differential as ABG was suggestive of metabolic acidosis. Anti-nuclear antibody (ANA) levels was sent as dRTA is found to be associated with Sjögren's syndrome. The ANA report came out positive with a titre of 1:120 speckled titre one positive. Thereby, an ANA profile was sent, which was positive for anti-Ro and anti-La antibodies. To confirm the diagnosis of Sjögren's syndrome, ophthalmologist's opinion was taken. Schirmer's test was performed, which was conclusive in favour of Sjögren's. Her right eye showed no signs of tears, (i.e., a very severe form of dry eye), and the left eye revealed severe dry eye (4 mm). Then patient was diagnosed as having primary Sjögren's syndrome with distal renal tublar acidosis causing hypokalaemic periodic paralysis, though she did not have any sicca symptoms in the past suggestive Sjögren's syndrome. Patient might have had cardiac arrest because of hypokalaemia only. Patient's attendants took discharge on request and did not come back for a follow-up visit; so further work-up could not be done.

Table I:

Lab tests	Patient 1	Patient 2
Haemogram (Hb/WBC/Plt)	10.5/7.7/84 k	10.2/12/336 k
ABG (pH, PCO2, HCO3, PO2, Lactate)	7.367, 28.1, 17.8, 1.2	7.1, 21.1, 10, 90, 3
Urine pH	5.7	6.0
ESR	90	43
Serum electrolytes ($Na^+/K^+/Cl$)	Day 1 - 141/2.1/113 Day 3 - 135/3.02/111 Day 5 - 136/3.15/110 Day 7 - 141/4.31/122	141/1.3/113
ANA by IFA	Positive 1:80 Speckled	Positive 1:120 Speckled
PBF	Microcytic hypochromic with anisopoikilocytosis in form of target cells	Microcytic hypochromic with anisopoikilocytosis
Viral markers (HBSAG, HIV 1&2, HCV)	Negative	Negative
LFT	WNL	WNL
RFT (blood urea, S. creatinine, S. uric acid)	19.6/0.8/3.1	57.3/2.8/9.8
S. iron	23.5	23.5
TSH	1.367	1.367
Urine R/E	WNL	WNL
ANA profile	SS-A/R060 KD SS-A/R052 KD SS-B/LA	SS-A/R060 KD SS-A/R052 KD SS-B/LA

Discussion

Systemic autoimmune disease Sjögren's syndrome is characterised by a distinct combination of signs and symptoms that are mostly brought on by a cell-mediated autoimmunity towards exocrine glands. Approximately 30 to 40 per cent of patients with primary Sjögren's syndrome experience systemic symptoms. The kidney is the non-exocrine organ most frequently impacted by Sjögren's syndrome. Distal renal tubular acidosis (dRTA) is the most typical type of renal involvement in Sjögren's syndrome. It is typically asymptomatic and goes unnoticed in most cases. Interstitial nephritis follows. The most frequent electrolyte imbalance in dRTA patients is hypokalaemia[4].

Distal RTA can occur on its own or as a subsequent consequence of other illnesses like chronic hepatitis, autoimmune disorders, and transplant rejection. For

autoimmune illnesses, the connection between Sjögren's syndrome and distal RTA is well known. The possible mechanism causing distal RTA is the lack of an H±ATPase pump in intercalated cells in the collecting tubules caused by immune-mediated injury, which may be the cause of distal RTA in Sjögren's syndrome[5]. This decrease in secretion and subsequent retention of hydrogen ions causes an increase in potassium excretion in exchange for sodium reabsorption in the collecting tubules to maintain electroneutrality. The other mechanism is a dysfunctional H±ATPase pump that causes sodium loss and, in turn stimulates the action of the hormone angiotensin-aldosterone, which results in hypokalaemia.

In our case series, patient 1 presented with paraparesis and patient 2 presented with quadriparesis; both their investigations revealed significant hypokalaemia and metabolic acidosis as the causes of the presenting complaint, and primary Sjögren's was suspected. All suspected instances of primary Sjögren's syndrome should be tested for the presence of anti-SSA antibodies (antibodies against Sjögren's syndrome-related antigen A), which are present in two-thirds of patients. In the absence of anti-SSA antibodies, a minor salivary gland biopsy is often advised to confirm a diagnosis of primary Sjögren's syndrome. A helpful test to determine ocular dryness is Schirmer's test. The latest and new American College of Rheumatology/European League Against Rheumatism ACR/EULAR established a new set of classification criteria for primary SS in 2016 which is enlisted in the Table II, and the diagnosis requires a minimum score of 4[6,7]. Both our patients met the criteria with a score of 4 (Anti-SSA/Ro, Schirmer's test positive), hence our diagnosis was confirmed.

Primary SS is treated symptomatically. When a patient with hypokalaemia appears in an emergency situation, the goal is to reverse the severe hypokalaemia with intravenous potassium supplementation, which treats the underlying acidosis. For the majority of patients, long-term potassium supplementation may be necessary. Muscarinic agonists are suggested for the treatment of mouth dryness and, to a lesser extent, ocular dryness. A combination of corticosteroids and other immunosuppressive medication has been claimed to reduce the course of renal impairment (tubular defects) in Sjögren's syndrome[8,9]. A more individualised strategy is required to enhance long-term outcomes in patients with primary SS due to the heterogeneity in the aetiopathogenesis and clinical manifestation of the disease, as well as a variable response to clinical treatments.

A score >4 classifies a patient who meets the including criteria and does not have any of the exclusion criteria.

Table II: The ACR/EULAR classification criteria for Primary Sjögren's syndrome 2016[6,7].

Item	Weight/Score
Labial salivary gland with focal lymphocytic sialadentitis and focus score of > 1 foci/4 mm^3	3
Anti-SS-A/RO positive	3
Ocular staining score > 5 in at least one eye	1
Schirmer's test < 5 mm/5 minutes in at least one eye	1
Unstimulated whole saliva flow rate < 0.1 mL/minute	1

Conclusion

Clinically Sjögren's syndrome may present differently in different patients. Patients presenting with renal symptoms as recurrent hypokalaemia as the initial presentation in Sjögren's syndrome pose much difficulty in diagnosis. This example serves as a reminder of the need to maintain a high index of suspicion for Sjögren's syndrome in patients presenting with recurrent hypokalaemia, especially middle-aged females.

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