DOI: 10.7860/JCDR/2022/56588.16722

Case Report

Internal Medicine Section

Recurrent Hypokalaemic Paresis in Secondary Sjögren's Syndrome

VIGNESSH RAVEEKUMARAN[1], DHRUVI REDDY SANIKOMMU[2], SIVASHANKAR[3]

ABSTRACT

Hypokalaemia has a wide scale of causes. The most common ones include potassium loss from urinary tract, gastrointestinal system and loss through sweating. This report is about a young 24-year-old Indian female who presented with sudden onset weakness of all four limbs which was found to be secondary to hypokalaemia. Refractory hypokalaemia and severe metabolic acidosis in this patient led to further work-up, which revealed positive Anti-SSA (anti-Sjögren's-syndrome-related antigen A autoantibodies), Anti-SSB Anti-Sjögren's syndrome type B and Anti-snRNP (Small nuclear ribonucleoprotein), strongly suggestive of secondary Sjögren's syndrome. Renal involvement with distal Renal Tubular Acidosis (RTA) causing hypokalaemia is seen in 10% of cases with Sjögren's syndrome. Thus, this report highlights the unusual initial presentation of hypokalaemic paresis in a patient with Sjögren's syndrome, and to emphasise that an autoimmune disorder should be considered in such presentations.

Keywords: Autoimmune, Potassium, Renal tubular acidosis, Weakness

CASE REPORT

A 24-year-old Indian female presented to the Emergency Department with history of vomiting and weakness of all limbs for one day. Her medical history revealed that she was diagnosed with hypothyroidism for two years for which she discontinued treatment after a few months. She reported history of diffuse abdominal pain, burning micturition and increased frequency of urination one week prior to admission. There was low-grade intermittent fever associated with chills, generalised myalgia and multiple joint pains. She had several episodes of vomiting in a day, and her generalised fatigue and myalgia worsened after which she suddenly developed weakness of all four limbs. She wasn't able to ambulate or do her daily activities. She did not have any other significant history.

On presentation, patient was conscious and oriented. Vitals-pulse rate 92 per min, blood pressure 70/40 mmHg, Saturation of Peripheral Oxygen (SpO_2) 97% on room air. General examination revealed mild bilateral swelling of hands. Her hypotension was treated with fluid challenge. Despite fluid challenge, patient's blood pressure did not improve. Inotropes were started accordingly. Neurological examination revealed hypotonia in bilateral upper limbs, decreased power of 3/5 in bilateral upper limbs and 2/5 in lower limbs. Deep tendon reflexes were preserved in all limbs, and sensations were intact.

Routine investigations revealed high anion gap hyperchloremic metabolic acidosis {pH-7.22, HCO_3-7, anion gap 16 (Normal range: pH 7.35-7.45, HCO_3 22-26 mEq/L, anion gap 8-12)}, severe hypokalaemia {serum potassium: 1.7 mEq/L (Normal range: 3.5-5.4 mEq/L)}, deranged creatinine-1.56 mg/dL (Normal range: 0.5-1.1 mg/dL), neutrophilic leukocytosis and presence of pus cells and occasional bacteria in urine routine. Alkaline urinary pH with elevated urine spot potassium was present. Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) were elevated {ESR 98 mm/hour, CRP 24 mg/L (Normal range ESR: <29 mm/hour; CRP <10 mg/L}. Thyroid profile was within normal range. ECG showed U waves in precordial leads.

Patient was provisionally diagnosed as hypokalaemic paresis. Potassium and bicarbonate correction were given. During the course of hospital stay, serum potassium and Arterial Blood Gas (ABG) were serially monitored [Table/Fig-1]. Inotrope support was tapered and stopped. Despite continuous correction, hypokalaemia and metabolic acidosis persisted. Due to elevated blood counts and pus cells in urine analysis, empiric antibiotics were started to treat a probable underlying urinary tract infection. Total blood counts and creatinine were monitored and were on an improving trend. Blood and urine cultures were sterile and antibiotics were discontinued.

Parameters	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
Serum K^+	1.7	1.9	2.5	3.6	2.3	3.2	3.5	5.1	4.9	3.8
pH	7.22	7.26	7.49	7.48	7.45	7.42	7.46	7.53	7.48	7.4
HCO_3	7	7	12	16	15	15	19	18	14	19
Creatinine	1.56	1.37	1.1	0.88	1.52	0.77	0.84	0.92	0.83	1.05
WBC	14100	15900	15900	15800	9500	6600	4900	5700	4000	4000

[Table/Fig-1]: Serial monitoring of serum potassium (mEq/L), ABG (pH mmHg, HCO_3 mEq/L), creatinine (mg/dL) and white blood cell counts (cells/mm^3).

The RTA was attributed to the refractory hypokalaemia and metabolic acidosis. In this patient with hypokalaemia, alkaline urine and positive urine anion gap (Value-243), distal RTA was more likely. Patient was evaluated further for underlying etiology. Anti-Nuclear Antibody (ANA) was highly positive with 1:1000 estimated titre; homogenous and speckled pattern. Anti-Phospholipid Antibody (APLA) profile was negative. ANA blot revealed positive Smith-Ribonucleotide protein (Sm/RNP) antibodies, Anti-Sjögren's Syndrome antigen A and B (SSA and SSB), Anti-Ro 52kD antibodies and weakly positive histone antibodies. This panel was highly suggestive of Secondary Sjögren's syndrome associated with a Mixed Connective Tissue Disorder (MCTD) [Table/Fig-2].

Test description	Observed value	Reference range	Disease association
Mi-2	Negative	Negative	Polymyositis, Dermatomyositis
Ku	Negative	Negative	SLE, Sjogren's, Scleroderma, MCTD
Sm/RNP	Positive +++	Negative	MCTD, Sharp syndrome
Sm	Negative	Negative	SLE
SSA	Positive +++	Negative	Sjogren's syndrome
SSB	Positive ++	Negative	Sjogren's syndrome, SLE
Ro 52kD	Positive +++	Negative	Sjogren's syndrome
Scl-70	Negative	Negative	Systemic sclerosis
PM-Scl 100	Negative	Negative	Overlap syndrome
Jo-1	Negative	Negative	Polymyositis, ILD
CENP-A/B	Negative	Negative	CREST syndrome

PCNA	Negative	Negative	SLE
dsDNA	Negative	Negative	SLE
Nucleosome	Negative	Negative	SLE
Histones	Weak positive +	Negative	Drug induced lupus, RA
Ribosome PO	Negative	Negative	SLE
AMA M2	Negative	Negative	Primary biliary cirrhosis

[Table/Fig-2]: ANA blot showing strongly positive Anti-Sm/RNP, SSA, SSB and Ro 52kD antibodies.
SLE: Systemic lupus erythematosus; MCTD: Mixed connective tissue disorder; ILD: Interstitial lung disease; RA: Rheumatoid arthritis

According to the revised international classification criteria for Sjogren's syndrome, Secondary Sjogren's syndrome was highly suspected with patient's prior history of dry eyes, positive Schirmer's test, and presence of autoantibodies along with underlying MCTD. MCTD fulfilled the diagnostic criteria with features of swollen hands, positive snRNP antibodies, mixed features of SLE and polymyositis (polyarthritis and muscle weakness). This unusual presentation of hypokalaemic quadriparesis was secondary to distal RTA that is a common extraglandular feature of Sjögren's syndrome seen in 10% of patients.

Patient was started on steroids (oral prednisone 10 mg per day) and received continuous correction of potassium and bicarbonate till normal values were achieved. Patient's power improved significantly and was discharged on day 10 of hospital stay with oral steroids (prednisone 10 mg/day), oral Disease Modifying Antirheumatic Drugs (DMARDs) such as hydroxychloroquine 200 mg per day and oral sodium bicarbonate. Patient was followed-up on outpatient basis weekly and steroids were tapered and stopped while hydroxychloroquine (HCQ) was continued.

Six months later, she once again presented with weakness in all limbs due to poor drug compliance. Neurological exam revealed power of 4/5 in all limbs, with normal tone and preserved deep tendon reflexes. Routine investigations showed compensated metabolic acidosis (pH 7.31 mmHg, pCO_2 19 mmHg, HCO_3 9 mEq/L) and hypokalaemia (serum potassium 2.4 mEq/L). Patient's weakness improved with potassium correction and she was symptomatically better by day three of admission. She was restarted on DMARDs and discharged with the same on day five of admission. She was regularly followed-up on outpatient basis monthly and she did not have any recurrence of symptoms again.

DISCUSSION

Serum potassium level below 3.5 mEq/L is considered as hypokalaemia. Severe hypokalaemia occurs when serum potassium level is <2.5 mEq/L. Hypokalaemia, depending on the severity, can affect several organ systems such as cardiovascular and neuromuscular systems. Most cases of moderate hypokalaemia are usually asymptomatic. Severe hypokalaemia, which is rare, can lead to mortality and morbidity. It can cause cardiac arrhythmias, skeletal muscle cramps, paralysis, hyporeflexia, and rhabdomyolysis [1].

Causes of hypokalaemia are: insufficient potassium intake, excessive discharge, or changes in the intracellular and extracellular potassium distribution. In endocrine diseases there is loss of potassium. Such endocrine diseases with renal potassium loss are-primary aldosteronism, congenital adrenal hyperplasia, Liddle syndrome, RTA and Bartter syndrome [2].

Abnormal sarcolemma excitability can cause episodic flaccid weakness resulting in a rare channelopathy called Hypokalaemic Periodic Paralysis (HPP). This may be caused by a transient shift of potassium into cells, as seen in HPP (caused by familial periodic paralysis or thyrotoxic periodic paralysis), or a larger deficit of potassium as a result of severe renal or gastrointestinal potassium loss [3]. In this case, severe hypokalaemia was attributed to renal potassium loss via distal RTA.

Even with the presence of decreased urinary acidification and hyperchloraemic metabolic acidosis, distal RTA was more likely due to alkaline urinary pH as compared to proximal type. Distal RTA can be primary (either idiopathic or inherited-medullary sponge kidney and Wilson's disease) or secondary. Secondary distal RTA occurs with calcium metabolism disorders (hyperparathyroidism, vitamin D intoxication and sarcoidosis), medications (ifosfamide, amphotericin B, lithium carbonate and ibuprofen) and autoimmune diseases (Sjögren's syndrome, Systemic Lupus Erythematosus (SLE) and rheumatoid arthritis) [1,3].

In this case, presence of hypokalaemia, hyperchloraemic metabolic acidosis, urinary pH of 6.5 and absence of a positive familial history were all suggestive for type 1 (distal) RTA secondary to Sjögren's syndrome. Patients with Sjögren's may have clinical and pathological evidence of both proximal and distal RTA. In healthy people, a negative urinary anion gap is seen since the chloride concentration exceeds that of sodium plus potassium [4]. The finding of positive urinary anion gap during acidosis, such as in this patient, was very reliable for the confirmation of the diagnosis of distal RTA.

Sjögren syndrome is an important cause of RTA. Sjögren syndrome is a systemic autoimmune disorder with predominant exocrine gland involvement leading to sicca symptoms and is characterised by chronic lymphocytic infiltration of salivary, lacrimal, and parotid glands. It is classified into primary and secondary based on the presence of underlying pathology [5]. In secondary Sjögren syndrome, there is an underlying pathology such as SLE, rheumatoid arthritis or MCTD. Renal manifestations are the most common extraglandular manifestations seen. Common renal presentations include tubular interstitial nephritis and RTA mild hypokalaemia associated with distal RTA is common in Sjögren syndrome, however, severe hypokalaemia causing paralysis is unusual [5]. In a similar case report, patient had developed quadriparesis which improved with potassium correction. However it was complicated with respiratory distress unlike the index case [6].

The exact mechanism by which Sjögren syndrome causes distal RTA is unknown. One proposed theory is the complete absence of H-ATPase pump in cortical collecting duct as described in some studies. Another possible mechanism which causes defective H^+ secretion is carbonic anhydrase 2 inhibition due to high titer of autoantibodies [5,7]. Reduced proximal sodium reabsorption secondary to metabolic acidosis causes severe hypokalaemia. The volume contraction causes raised levels of distal sodium and aldosterone activity resulting in further potassium excretion. Distal RTA induced hypokalaemia is a late presentation, reported in <2% of Sjogren's syndrome cases [8].

Treatment of RTA in Sjögren's syndrome includes potassium restitution and bicarbonate replacement (0.5-2 mmol/kg in four divided doses) [9]. Hydroxychloroquine (200 mg daily) is helpful in arthralgias and mild arthritis. Steroids and monoclonal antibodies appear to be effective in patients with systemic disease, particularly those with purpura, arthritis, fatigability, and in refractory cases. In a study, patients who had distal RTA as initial presentation in Sjögren's syndrome were compared and it was noticed that majority of patients received symptomatic treatment and improved clinically with the same [9]. In another study, good response to steroid therapy was seen in a patient with similar presentation [10]. Likewise, this patient was treated with DMARDs such as hydroxychloroquine and low dose steroids along with potassium and bicarbonate supplements. There was an overall good clinical outcome in this patient, with improvement of muscle power and fatigability. She did not have any further episodes of paresis or acidosis on follow-up.

CONCLUSION(S)

The diagnosis of Sjögren's is challenging to clinicians, particularly when the initial presentation differs from the exocrine manifestation

of dry eyes and mouth. This case is reported to highlight the unusual initial presentation of hypokalaemic paresis in a patient with Sjögren's syndrome, and to emphasise that an autoimmune disorder should be considered in such presentations. Diagnosis at an early stage may allow better control and prevent progression of disease. Some cases get complicated with tubulointerstitial nephritis and worsening of renal parameters with poor prognosis. Early initiation of steroids in this patient showed improvement in renal parameters, with overall good outcome.

REFERENCES

[1] Celik M, Ayturk S, Mert O, Kucukarda A, Kurultak I, Donmez S, et al. Patient with type 1 distal renal tubular acidosis secondary to Sjogren's syndrome presented with hypokalemic paralysis. J Med Cases. 2015;6(6):268-70.

[2] Zhou Y, Huang N, Cao G, Luo Y. Type I renal tubular acidosis caused by Sjögren's syndrome with hypokalemia as the first symptom: A case report. J Int Med Res. 2020;48(2):0300060519880765.

[3] Sinha U, Sengupta N, Sinharay K, Sahana PK. Recurrent hypokalemic paralysis: An atypical presentation of hypothyroidism. Indian J Endocrinology and Metabolism. 2013;17(1):174-76.

[4] Morović-Vergles J, Galešić K, Vergles D. Primary Sjögren's syndrome presenting as hypokalemic paralysis. Ann Saudi Med. 2007;27(2):125-27.

[5] Meena DS, Kumar D, Bohra GK, Bhambu SK. Hypokalemic paralysis as an initial presentation of Sjogren syndrome. Ann African Med. 2020;19(2):147-49.

[6] Gupta S, Gupta S, Ravjani N. Hypokalemic periodic paralysis and renal tubular acidosis as presenting manifestation of primary Sjogren's Syndrome-A case report. The Indian Practitioner. 2020;73(6):47-49.

[7] Soleimani M, Rastegar A. Pathophysiology of renal tubular acidosis: Core curriculum 2016. Am J Kid Dis. 2016;68(3):488-98.

[8] Agrawal S, Bharti V, Jain MN, Purkar PD, Verma A, Deshpande AK. Sjogren's syndrome presenting with hypokalemic periodic paralysis. J Assoc Physicians India. 2012;60:55-56.

[9] Garza-Alpirez A, Arana-Guajardo AC, Esquivel-Valerio JA, Villarreal-Alarcón MA, Galarza-Delgado DA. Hypokalemic paralysis due to primary Sjögren syndrome: Case report and review of the literature. Case Reports in Rheumatology. 2017;2017

[10] Muthukrishnan J, Dawra S, Marwaha V, Narayanan CS. Sjögren's syndrome presenting as hypokalemic paralysis. Medical Journal, Armed Forces India. 2015;71(Suppl 1):S172-74.

PARTICULARS OF CONTRIBUTORS:

1. Resident, Department of Internal Medicine, Mahatma Gandhi Medical College and Research Institute, Puducherry, India.
2. Resident, Department of Internal Medicine, Mahatma Gandhi Medical College and Research Institute, Puducherry, India.
3. Assistant Professor, Department of Nephrology, Mahatma Gandhi Medical College and Research Institute, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Dhruvi Reddy Sanikommu,
Resident, Department of Internal Medicine, Mahatma Gandhi Medical College and Research Institute Campus, Pillayarkupam, Puducherry, India.
E-mail: dhruvi.reddy24@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Apr 05, 2022
- Manual Googling: May 23, 2022
- iThenticate Software: Jun 07, 2022 (20%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 27, 2022**
Date of Peer Review: **Apr 25, 2022**
Date of Acceptance: **May 24, 2022**
Date of Publishing: **Aug 01, 2022**