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Hypokalaemic paralysis due to underlying distal renal tubular acidosis as the first presentation of primary Sjogren's syndrome: a case report

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Abstract

Sjögren syndrome is a systemic autoimmune disease that primarily affects the exocrine glands. A 36-year-old woman presented with sudden onset of bilateral lower limb weakness. She was noted to have hypokalaemia with a normal anion gap metabolic acidosis. Subsequent investigations revealed high ESR, positive ANA, absent dsDNA, normal C3, C4, positive anti-Ro and negative anti-La. Labial biopsy revealed a lymphocytic infiltrate and renal biopsy revealed tubulointerstitial nephritis. Sjogren's syndrome rarely (less than 5%) presents for the first time as renal manifestations such as hypokalaemia related paralysis as a result of type I – distal renal tubular acidosis due to the underlying tubulointerstitial nephritis.

Key words: hypokalaemic paralysis, primary Sjogren's syndrome, type 1 - distal renal tubular acidosis

Introduction

Hypokalaemia-related paralysis secondary to an underlying renal, endocrine or iatrogenic cause leads to muscle weakness and they have persistently low levels of potassium even between attacks of muscle weakness, which is different from familial and periodic forms of hypokalaemic paralysis.(1) Type I - distal renal tubular acidosis (type I - dRTA) is impaired acid excretion by the collecting duct system, which is characterised by the failure to acidify urine below pH 5.5, leading to metabolic acidosis and hypokalaemia. (2) Sjögren syndrome is a systemic autoimmune disease that primarily affects the exocrine glands, such as salivary and lacrimal glands, and results in the severe dryness of mucosal surfaces, principally in the mouth and eyes and is known to be associated with renal manifestations such as renal tubular acidosis due to an underlying tubulointerstitial nephritis. However it is rarely seen as a first presentation.(3) We present a patient with hypokalaemic paralysis due to underlying type I - dRTA as the first presentation of primary Sjogren's syndrome.

Case presentation

A 36-year-old woman, mother of two children presented with bilateral lower limb weakness and muscle pain for the preceding two to three days duration, worsening over the last day preceding the admission. She had progressive difficulty in walking and had fallen whilst attempting to walk immediately before the admission. She had no mouth deviation, upper limb weakness, blurred or double vision, urinary incontinence, bowel incontinence, or sensory symptoms. She denied a history of a recent

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respiratory or gastrointestinal infection, large carbohydrate-rich meals, strenuous exercises, recent intake of any diuretics, recreational drugs or herbal concoctions, symptoms of an underlying hypothyroid and thyrotoxic state or a past history or family history of similar presentations or pregnancy or foetal morbidity. She denied any history of renal colic or renal stone disease or a family history of renal disease. On close questioning, she gave a history of mild dry mouth for about 3 months but denied any eye irritation, dry eyes or dyspareunia. She denied any other symptoms of an underlying autoimmune or connective tissue disorder. She also denied urinary symptoms such as polyuria, gastrointestinal, respiratory or cardiac symptoms.

On examination, there was bilateral upper and lower limb weakness with modified medical research council (mMRC) power of grade 2, with present but reduced reflexes of the bilateral upper and lower limbs. Sensations were intact in the bilateral lower limbs, perianal and sacral areas. Cerebellar signs were negative. The anal tone was normal. There were no spinal deformities and tenderness. Her general, cardiovascular, respiratory, gastrointestinal and genitourinary examinations were normal.

The haematological, biochemical, histological and imaging investigations are shown in table 1. Her initial electrolytes revealed evidence of severe hypokalaemia (K+ - 1.8 mmol/L) with evidence of metabolic acidosis with a -Bicarbonate level of 10 mmol/L on admission. Her urine potassium was 18 mmol/L when her serum K+ was 2.9 mmol/L, which, considering the serum and urine osmolarity, revealed a trans-tubular potassium gradient (TTKG) of 5, indicating evidence of renal potassium wasting. This showed evidence of type 1 – distal renal tubular acidosis. Her ANA was positive at a titre of 1:80 (nuclear pattern), dsDNA was negative, C3 and C4 were normal, Rheumatoid factor (RF) was negative, Anti Ro was positive and Anti La was negative. Her labial biopsy revealed evidence of lymphoplasmacytic infiltrate in the salivary parenchyma, including prominent periductal distribution. Renal biopsy revealed that tubules show mild tubular inflammation and occasional protein casts. A mild mixed inflammatory cell infiltrate including lymphocytes and neutrophils was seen in the interstitium. Mild tubular interstitial nephritis was noted. Based on the American College of Rheumatology -European League Against Rheumatism (ACR-EULAR) 2016 classification criteria, she was diagnosed with Sjogren's syndrome.(3)

She was commenced on intravenous potassium chloride via a central line. Her limb weakness improved after potassium replacement. The hospital stay was complicated by hospital-acquired pneumonia and provoked deep vein thrombosis due to the central venous line inserted into the right femoral vein. Subsequently she was put on oral potassium replacement, oral sodium bicarbonate (NaHCO3), hydroxychloroquine and oral anticoagulation (warfarin). She is currently being followed up at the Nephrology, Rheumatology and Medical clinics in the hope of commencement of oral glucocorticoids.

Discussion

Hypokalaemia is a cause of bilateral upper and lower limb weakness. However the underlying cause of hypokalaemia needs to be evaluated as in our case which led to the eventual diagnosis of type I – dRTA due to underlying tubulointerstitial nephritis as a result of primary Sjogren's syndrome.

There are a multitude of causes for hypokalaemia, type I – dRTA and tubulointerstitial nephritis. Hence we need to rule out both common and uncommon diagnoses.(4) There are a handful of case reports on patients with Sjogren's syndrome who presented with quadriparesis and limb weakness as their initial presentation. In most cases there has been a significant lag time in diagnosing the underlying cause for hypokalaemia and type I – dRTA such as Sjogren's syndrome as the overt clinical manifestations evolve over time.(5) The most common renal manifestation of Sjögren's syndrome is tubulointerstitial nephritis, which may present as type I - dRTA; it accounts for 7.1-19.2% of cases who present with renal potassium wasting or hypokalaemic paralysis which is similar to our patient. However it is most often a retrospective diagnosis rather than a prospective one.(4) Hence symptoms related to RTA should trigger the search for conditions such as Sjogren's syndrome even when there are minimal sicca symptoms. About one third of patients present with systemic extraglandular manifestations such as the above and can be the primary presentation of primary Sjogren's syndrome. The spectrum of the renal disease includes interstitial nephritis, which can manifest as distal RTA, proximal RTA, tubular proteinuria, nephrogenic diabetes insipidus, glomerular diseases, or renal failure.(6)

Hence, it is important to evaluate an underlying cause for the hypokalaemia with distal renal tubular acidosis because many patients with early Sjogren's syndrome will have very little clinical features to support the diagnosis at the onset as in the case of

Table 1 - Haematological, biochemical, histological and imaging investigations

Investigation	Value	Reference range
pH	7.179	7.35-7.45
HCO_3^- (mEq/L)	9.8	20-22
BE	-15	-2-+2
pCO2 (mmHg)	21.5	40
pO2 (mmHg)	60.5	60-100
Na^+ (mmol/L)	140	135-145
K^+ (mmol/L)	1.83	3.5-4.5
Cl^- (mmol/L)	120.5	96-106
Anion gap	10	8-12
Delta ratio	0.63	
RBS (mg/dL)	96	<100
Serum ketone bodies	Negative	
CPK (U/L)	97	29-168
WBC (x 10^9/L)	7	4-10
Neutrophil (x 10^9/L)	4.58	2-7
Lymphocytes (x 10^9/L)	1.57	0.8-4
Haemoglobin (mg/dL)	10.4	11-16
Platelet (x 10^9/L)	365	157-371
APTT	31	21-34 s
PT/INR	13.9/1.12	11.5-15.5 (<1.5)
LDH (U/L)	139	140 - 280
Serum osmolarity (mOsm/Kg)	294	285 – 295
Urine osmolarity (mOsm/Kg)	385	50 – 1400
Urine Na^+ (mmol/L)	150	<20
Urine K^+ (mmol/L)	18	0 – 10
Transtubular potassium gradient (TTKG)	5 (with a serum K + of 2.9)	
Hep B	Negative	
Hep C	Negative	

Table 1 - Haematological, biochemical, histological and imaging investigations (continued)

Investigation	Value	Reference range
HIV	Negative	
Calcium (mg/dL)	8.0	8.5 - 10
PO_4^{3-} (mg/dL)	2.6	2.5 – 4.5
Magnesium (mg/dL)	1.8	2-4
TSH (mU/L)	0.659	0.35 – 4.94
T4 (ng/dL)	0.77	0.7 – 2.0
9.00 AM cortisol (nmol/L)	359	118 – 618
Total protein (g/dL)	7.1	
Albumin (g/dL)	2.7	
Globulin (g/dL)	4.4	
Urine pH	6.5 – 7.0 (With ongoing systemic acidosis)	4.5 – 7.8
Red cells in Urine	Nil	
Pus cells in Urine	Nil	
S. Cr (mg/dL)	0.82	0.57 – 1.11
eGFR	92	
AST (U/L)	30	5-34
ALT (U/L)	15	0 – 55
Total Bilirubin (mg/dL)	0.9	0.2-1.2
Blood picture	Normal	
uPCR	1.24	<0.2
CRP (mg/L)	6	<6
ESR (mm/1st hour)	120	<20
CXR	Normal	
USS KUB	Normal. No evidence of nephrocalcinosis	
CECT	Normal	
R/S Lower limb doppler	Right side lower limb deep vein thrombosis	
2D Echocardiogram	Normal	
ECG	Initial long QT – subsequently normal	

Table 1 - Haematological, biochemical, histological and imaging investigations (continued)

Investigation	Value/ Result
Rheumatoid factor	Negative
ANA	1:80 positive
dsDNA	Negative
C3	Normal
C4	Normal
Anti Ro (SSA)	Positive
Anti La (SSB)	Negative

our patient but early serological testing along with labial and renal biopsy enabled us to conclusively diagnose the patient so that early treatment could be commenced to prevent progressive renal injury and recurrent attacks of limb weakness.

Conclusion

It is important that we evaluate the underlying cause of hypokalaemia related paralysis so that the underlying condition is treated in order to prevent the recurrence of similar episodes of weakness in the future and also detect the underlying disease entity such as Sjogren's syndrome even when there are few symptoms to prevent progression of the underlying disease.

Declarations

Author contributions
All authors contributed to the acquisition of data. All contributed to writing the manuscript. All authors read and approved the final manuscript.

Conflicts of interest
The authors declare that they have no conflicts of interest to be addressed regarding this case report.

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