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A Rare Renal Twist in Sjögren Syndrome: Type I RTA

Mujeeb ur Rehman, Muhammad Irfan, Shahneela Tabassum, Muhammad Nasir

ABSTRACT

Sjögren's syndrome (SS) is an autoimmune condition that causes chronic inflammatory and degenerative changes in exocrine glands and systemic organs. Rare in adolescents, it often goes undiagnosed due to absent xerostomia, xerophthalmia, or sicca symptoms. Adolescents may initially present with parotitis or systemic organ involvement. We report a 36-year-old woman with recurrent severe hypokalemic episodes since age 21, ultimately diagnosed with type I (distal) renal tubular acidosis (RTA) due to SS. Despite significant hypokalemic paralysis in her background, the diagnosis was delayed as distal RTA is rare in this age group. The diagnosis was confirmed following severe hypokalemia, non-anion gap metabolic acidosis, raised urine anion gap and pH, supported by autoimmune workup. She was successfully managed with potassium and alkali replacement therapy, which stabilized her condition. This case highlights diagnostic challenges of SS when initial symptoms deviate from typical exocrine manifestations.

Key words: Hypokalemia, Renal Tubular Acidosis, Sjögren Syndrome.

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INTRODUCTION

The inability of the renal tubules to maintain the proper balance of physiologic acid-base is the hallmark of renal tubular acidosis (RTA). It frequently arises from a malfunction in tubular transporters which are involved in the secretion or absorption of certain ions as a result of autoimmune diseases, nephrotoxic medication exposure, diuretic usage, congenital conditions or malignancy (e.g. multiple myeloma). The three primary types of RTA are hyperkalemic or type 4, proximal or type 2 and distal or type 1. All three types of RTA are characterized by anomalies in serum potassium levels (hypo- or hyperkalemia), an alkalotic or acidotic urine pH, a positive urine anion gap, and hyperchloremic non-anion gap metabolic acidosis.

This case report focuses on distal RTA (also known as type 1 or classic RTA), which is further characterized by significant hypokalemia (<3 mmol/L) and an alkalotic urine pH (>5.5). It is frequently brought on by a malfunction in the distal renal alpha-intercalated cells' ability to secrete hydrogen ions. Thus, ionic wasting results from a compromised luminal gradient, which may cause rickets/ osteomalacia, nephrocalcinosis, nephrolithiasis, respiratory failure and muscle weakness. Adolescents with SS may experience distal RTA infrequently, but research has shown that tubulointerstitial nephritis causes abnormalities in distal tubular acidification in a larger percentage of adult patients.[1] The case being reported is of a middle aged lady who came up with hypokalemic periodic paralysis, actually was suffering disease since adolescence, ultimately diagnosed with distal RTA as a cause of hypokalemia and subsequently revealed its association with SS. The patient was successfully treated with potassium and alkali replenishment that led to complete resolution of symptoms and improvement in investigational findings.

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Case Presentation

36 years of age, female, known case of well controlled hypothyroidism, having very significant history of hospitalizations on various occasions in last fifteen years for hypokalemic periodic paralysis, was admitted in hospital for video-assisted thoracoscopy for Empyema thoracis. After few hours of procedure completed, she developed sudden-onset weakness of all four limbs. The patient stated that her symptoms resembled those of her earlier/ previous attacks. Systemic review revealed no signs of syncope, gastrointestinal distress, urinary complaints, joint discomfort and rash, overuse of diuretics or laxatives, suicidal or homicidal thoughts. Family history revealed no ongoing autoimmune

disorders. She denied drinking or smoking. For her probable tuberculosis, the woman was receiving anti-tuberculous medication in addition to her potassium chloride regimen.

Her neurological examination revealed normal bulk, lower limb power of 2/5, upper limb power of 3/5, decreased reflexes, and downgoing plantars. Rest of clinical examination were unremarkable. Her serum sodium was138 mmol / L, potassium 1.8 mmol / L, chloride 112 mmol / L, bicarbonate 14.6 mmol / L and blood pH was 7.26, urine sodium 104 mmol / L, urine potassium 25.12 mmol / L, and urine chloride 99 mmol / L. Urinalysis showed pH of 7.0 without blood or protein (Table 1). Ultrasound KUB revealed bilateral nephrolithiasis. On the ECG, U waves, delayed intraventricular conduction, and sinus bradycardia were observed. She was diagnosed with distal RTA due to hyperchloremic non-anion gap metabolic acidosis and a positive urine anion gap of 30.12. In addition to receiving potassium citrate and sodium bicarbonate, she was hydrated with intravenous normal saline, which resolved her hyperchloremic non-anion gap metabolic acidosis and hypokalemia. Upon her discharge from hospital, she was prescribed with oral potassium citrate and sodium bicarbonate. After three months of treatment, she remained asymptomatic with normal potassium and no acidosis.Before this presentation, she had episodes of acute paralysis on low serum potassium and was treated by general practitioner with IV and oral potassium but was not worked-up. No history of sicca symptoms in past and at present.

Antinuclear antibodies (ANA) (1:388) and anti-Ro / SSA antibodies (SSA - 52: 17.45 U / mL and SSA - 60: 16.28 U / mL) were positive in her autoimmune profile and she was borderline positive for anti-La / SSB. Anti-double-stranded DNA (dsDNA), anti-Smith, and anti-U1-ribonucleoprotein (RNP) antibodies were negative (Table 1). Fanconi syndrome, Bartter syndrome, and Gitelman syndrome were excluded from list of causes for renal tubulopathies. Patient could not be investigated for genetic/ molecular parameters because of financial constraints. A preliminary diagnosis of Sjögren's syndrome (SS) was made in light of a positive autoimmune panel. She now sees a rheumatologist and a nephrologist on a regular basis.

DISCUSSION

Type 1 renal tubular acidosis affects the distal nephron making it unable to lower the pH of urine. It is possibly to inherit or acquire type 1 RTA. Autoimmune conditions such as systemic lupus erythematosus, sarcoidosis and SS are linked to type I RTA.[2] Possible pathophysiological mechanism described to the occurrence of hypokalemic paralysis due to primary SS is based on proposed assumption for presence

Table 1: Laboratory Results of Patient

Laboratory markers	Results	Reference ranges	Values after treatment
Serum Markers			
Sodium	138.0	135 – 145 mmo l /L	
Potassium	1.8	3.5 – 5.0 mmol / L	4.5
Chloride	112.0	95 – 105 mmol / L	98
Bicarbonate	14.6	22.0–26.0 mmol/L	23.6
Urine electrolytes			
pH	7.0	4.5 – 7.8	5.2
Sodium	104.0	< 20 mmol / L	38
Potassium	25.12	< 15 mmol / L	12
Chloride	99.0	14 – 50 mmol / L	64
Anion gap	30.12	< 10 mEq / L	
Venous blood gas			
pH	7.26	7.31 – 7.41	7.37
Autoimmune panel			
ANA	1:388	< 1:80	
Anti-dsDNA	Negative	< 20.0 AU / mL	
Anti-Smith	Negative	< 10 U / mL	
Anti-Ro/SSA-52	17.45	< 10 U / mL	
Anti-Ro/SSA-60	16.28	< 10 U / mL	
Anti-La/SSB	Borderline positive	< 10 U / mL	
Anti-U1-RNP	Negative	< 10 U / mL	

ANA: antinuclear antibody; anti-ds DNA: anti-double-stranded DNA antibody; anti-SSA: anti-Sjögren's syndrome-related antigen A; anti-SSB: anti-Sjögren's syndrome-related antigen B; anti-U1-RNP: anti-U1 ribonucleoprotein antibody

of antibodies against H+-ATPase and carbonic anhydrase enzymatic pumps that lead to a positive urinary anion gap and a urine pH > 5.5.[3] Typically, distal RTA manifests as normal anion gap acidosis and mild hypokalemia. However, the literature has only reported a few number of cases of severe hypokalemia in distal RTA that led to muscle paralysis.[4] Numerous extra-glandular symptoms can accompany SS; two typical renal manifestations are renal tubular dysfunction and tubulointerstitial nephritis resulting in distal renal tubular acidosis.[5] In literature, the rare presentations of distal RTA due to SS has been reported in different ways. Some patients have reported with sicca symptoms while many remain asymptomatic and presents with unusual symptomatology like hypokalemia which is considered most prevalent electrolyte imbalance in distal RTA patients. Chinmaye S et al reported a case that was challenging to be diagnosed as a case of distal RTA due to SS as the hypernatremia masked usual clinical presentation though the reported patient was having hypokalemia and acidosis as well.[6] Therefore, diagnosis SS is challenging particularly when it initially presents with renal rather than exocrine manifestation.

Our patient had recurrent hypokalemic paralysis since adolescence, but the rare distal RTA remained undiagnosed. Hypokalemia rarely results in quadriplegia with imminent respiratory failure, however it can present with polyuria and polydipsia.[7] Hypokalemia may be initial presentation of distal RTA complicated with SS. Meena DS et al also intimated a case with same presentation of hypokalemic paralysis but patient was suffering from dryness of eyes and mouth and further diagnosis was confirmed with positive Schirmer test. [8] In this case severe hypokalemia, non-anion gap metabolic acidosis, raised urine anion gap and pH led to the diagnosis of SS confirmed by autoimmune workup. Diagnosing such cases is challenging, as they often don't meet criteria; our patient lacked sicca symptoms and other diagnostic features.

Despite the fact that muscle weakness has occasionally been reported as an SS presenting characteristic, clinicians rarely initially link muscle weakness with SS because the other factors are taken into consideration when evaluating patients who exhibit muscle weakness. In order to assess the clinical phenotype of primary Sjögren's syndrome (PSS) patients who presented with hypokalemic paralysis, Nahar N et al. performed a retrospective cross-sectional study. They discovered that 61.5% of patients experienced multiple episodes of hypokalemic paralysis, 69% experienced dry eyes, and 23% had inflammatory arthritis and 1 patient had Raynaud's phenomenon, myopathy.[9] Boro H et al described a case series and highlighted that how severe forms of distal RTA have bone mineral disorders that leads to deforming joints and easily breakable bones with minimal traumatic injuries. This results from exaggerated osteoclastic bone resorption due to untreated acidosis in RTA.[10] Our patient had developed hypocalcemia, hypercalciuria and subsequent nephrolithiasis but before bone mineral disorder may have emerged, diagnosis of disease has been made and successfully treated that led to reversal of these parameters.

CONCLUSION

With the current diagnostic criteria, it may be challenging to detect and diagnose SS early, increasing the risk of a missed/ delayed diagnosis. Patients may present with a range of symptoms that differ from the typical presentation of the condition. Most of the times, unusual presentations are overlooked but whenever recurrence of same presentation of symptoms is observed then it is deemed necessary to investigate those thoroughly to reach at exact root cause. Association of presenting symptoms coupled with laboratory and imaging parameters may surface exact pathological disturbance that may guide to ascertain exact cause like in current case. Therefore, to prevent potentially deadly results, patients who develop persistent or recurrent hypokalemia should receive prompt therapy for metabolic abnormalities using potassium and alkali medications and undergo further investigations to rule out SS.

Authors Contribution:
Mujeeb ur Rehman: Conception/ Study design, Acquisition of data, Manuscript drafting, Given final approval of version to be published
Muhammad Irfan: Conception/ Study design, Acquisition of data, Manuscript drafting, Given final approval of version to be published
Shahneela Tabassum: Conception/ Study design, Acquisition of data, Manuscript drafting, Given final approval of version to be published
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