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Case Study

A DIAGNOSTIC DILEMMA: RECURRENT HYPOKALEMIC WEAKNESS SECONDARY TO SJOGREN'S SYNDROME (A DRTA EFFECT)

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ABSTRACT

Renal involvement occurs in approximately 5% of patients with Sjogren's syndrome (SS). Renal lesions that predominate are tubulointerstitial nephritis and membranoproliferative glomerulonephritis. We report the case of a 50-year-old female who presented with weakness of lower limbs. A diagnosis of distal renal tubular acidosis type 1 (DTA1) secondary to SS was made, discovered in view of hypokalemic paralysis. The patient was treated symptomatically with injectable potassium chloride sodium bicarbonate. Corticosteroid and hydroxychloroquine were used to treat SS. The patient improved with correction of acidosis and hypokalemia.

Keywords: Sjogren's syndrome (SS), Hypokalemic paralysis, Renal tubular acidosis, Nephrolithiasis

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INTRODUCTION

Sjogrens syndrome (SS) is a systemic chronic inflammatory disorder characterised by CD4 T cells and B cells infiltration in exocrine organs (predominately Th1 cells rather than Th17) with single a single endocrine organ (autoimmune thyroiditis). It's an autoimmune exocrinopathy in which periductal and perivascular infiltrations occur, which leads to activation of ductal epithelium, leading to immune destruction of acini. Symptoms most commonly associated are keratoconjunctivitis sicca (dry eyes) and xerostomia (dry mouth). Extra glandular manifestations are Raynaud's phenomenon, vasculitis, interstitial lung disease (NSIP), lympadenopathies, renal involvement, peripheral neuropathy, gastrointestinal symptoms such as dyspepsia, diarrhoea, and constipation [1, 2]. Primary Sjogren's syndrome (pSS) has been called autoimmune epithelialitis.

CASE REPORT

A 50 y old female went to an outside hospital with complaints of progressive weakness in lower limbs. Not associated with vomiting, diarrhoea, and fever. The physical examination showed hypotonia and areflexia. The rest of the systemic examination was unremarkable. She also complained of fatigue, dryness of eyes and dryness of mouth. On admission, the patient's vitals were: blood pressure at 120/80 mm Hg, pulse at 88 beats/min, and temperature at 36.6 °C. There was no focal neurological deficit. All the biochemical markers were checked. (Table 1) Arterial blood gas analysis revealed severe metabolic acidosis with normal anion gap. In light of her severe hypokalemia with a normal anion gap metabolic acidosis, she was diagnosed with renal tubular acidosis and started on intravenous potassium.

Table 1: Biochemical markers

CBC	10.9/10,000/3.59
ESR	12 mm/h
CRP	4.94 mg/l
URINE ROUTINE MICRO	+1 Albumin
SERUM POTASSIUM	1.9 mmol/l
SERUM SODIUM	140 mmol/l
SERUM CHLORIDE	110 mmol/l
UREA	32
SERUM CREATININE	1.3 mg/dl
URIC ACID	3.4 mg/dl
RA FACTOR	<10
HCO3	20
SERUM MAGNESIUM	2.41
URNIARY SODIUM	99
URNIARY POTASSIUM	56.3
URNIARY ANION GAP	41 mEq/l
PLASMA ANION GAP	10
PLASMA OSMOLARITY	293 mOsm/kg
SERUM TSH	2.20

The patient had a history of recurrent hospitalisations for paraparesis secondary to the hypokalemic crisis in previous 2 years, which had improved with correction of hypokalemia, however, she was never investigated further as to the cause of hypokalemia. She had no family history of kidney disease. The DTPA scan revealed normal function in the right kidney, with prompt perfusion, cortical

extraction, and adequate clearance of the tracer. In contrast, the left kidney showed reduced perfusion and cortical extraction of the tracer, along with a delayed intra-renal transit time. The time-activity curve was low and flat, and faint tracer activity was detected in the nephrostomy bag, indicating significantly impaired renal function in the left kidney. The ultrasound of the abdomen and pelvis revealed multiple altered echotexture areas in the cortex of the left kidney, along with a prominent left renal pelvi-calyceal system containing internal moving echoes, indicative of pyelonephritis with pyonephrosis. Additionally, the presence of left renal calculi was noted. The liver was found to be mildly enlarged (mild hepatomegaly), and gallstones (cholelithiasis) were also detected. For which left PCN was done and 50 ml of pus was drained.

We had retained the diagnosis of primary SS because she had a score according to the 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary SS at 4 (The Schirmer test positive [score = 1], and anti-SSA/Ro positive [score = 3]), (table 2) and she had no exclusion criteria. Primary SS was identified as the cause of type 1 renal tubular acidosis.

Table 2: Autoimmune Workup

Ana titre-IFA	**1:100 (normal<1:40)**
Pattern	Granular speckled pattern seen
SS-A	Positive (50 intensity)
Ro 52 recombinant	76
Schirmer test	Positive (3 mm in right eye and 2 mm in left eye per 5 min)

The patient received symptomatic treatment with injectable potassium chloride, sodium bicarbonate, hydration, a low protein diet. In terms of etiological treatment, she was given corticosteroids and hydroxychloroquine. The outcome was favourable, with correction of acidosis and hypokalemia. She improved with these measures, and her power in lower limbs recovered. She was discharged with oral potassium and bicarbonate supplements and on discharge her serum potassium levels were 4.2.

DISCUSSION

Sjogren's syndrome is a chronic autoimmune inflammatory disease of the exocrine glands, characterized by keratoconjunctivitis sicca and xerostomia. It is frequently associated with connective tissue disease. Among the extra glandular manifestations of Sjogren's syndrome are various forms of renal disease, including renal tubular acidosis [2, 3]. Hypokalemia is known to be associated with renal tubular acidosis, and may manifest itself by muscle weakness, usually of a mild chronic character [4]. Type 1-Distal RTA characterised by failure of alpha intercalated cells of the medullary collecting duct to secrete $H^+$and reclaim K^+, Type 2—Failure of proximal tubular cells to reabsorb $HCO3^-$and Type 4 due to aldosterone deficiency or resistance [5].

The collecting tube is the site where regulation of urinary acid excretion takes place, and the type A intercalary cells in this segment perform the functions of distal H+ion secretion and HCO3 reabsorption. The secretion of $H^+$is affected by the H^+-ATPase and H^+-K^+-ATPase pumps. The proton secretion activity is coupled with HCO3 reabsorption activity carried out by the basolateral Cl^-/HCO3 exchanger, also called AE1. The Cl^-ion which enters the cell through the activity of the AE1 exchanger, is recycled via the basolateral K^+-Cl^-cotransporter. Defective type A intercalary cell function will result in hyperchloremic acidosis with a urinary pH unsuitable for acidosis (>5.5) and insufficient net acid excretion. In normal conditions, alkaline urine (pH>7.6) stimulates the secretion of H+. Hyperchloremic acidosis is associated with hypokalemia, hypercalciuria, bone disease (rickets/osteomalacia). Hypokalemia is explained by stimulation of distal potassium secretion by unabsorbed bicarbonate and stimulation of the renin-angiotensin-aldosterone system secondary to sodium loss. Chronic acidosis stimulates proximal reabsorption of citrate and bone resorption; hypocitraturia, alkaline urine, and hypercalciuria will lead to nephrocalcinosis, or nephrolithiasis. The pathogenesis of renal involvement and the pathophysiology of DTA1 during SS are still unclear [6], and probably multifactorial [7].

Kidney disease can be the consequence of tubulointerstitial infiltration of T cells, B cells, and plasma cells and, more rarely, of autoantibodies [8, 9]. The patients exhibit clinical manifestations that are due to interstitial infiltration of lymphocytes, which promotes interstitial fibrosis, leading to chronic kidney disease. Tubulitis has also been associated with distal DTA and leads to the complete absence of H+-ATPase in the collecting ducts [9, 10] and thiazide-sensitive NaCl cotransporter [8]. Autoantibodies to carbonic anhydrase were found in the serum of patients with lupus erythematosus systemic and SS and were also detected in the renal distal tubules [11]. Whether these autoantibodies are a consequence of, or contribute to, renal injury is not clear, although the induction of antibodies to carbonic anhydrase in mice can reproduce DTA [12]. The diagnostic delay that is observed in our patient is due to the fact that clinicians are not used to further exploration for hypokalemia and the absence of obvious extra-renal signs of SS. The clinical manifestation is also characterised by repetitive episodes of hypokalemic crisis with paralysis of the limbs, which often constitutes a differential diagnosis with Westphal's disease and thyrotoxic hypokalemic paralysis. It is clear that corticosteroid therapy is not effective on lesions of chronic tubulointerstitial nephropathy. However, DTA1 is mainly attributed at the etiopathogenetic level to immunological phenomena and not to organic tubulointerstitial involvement. Therefore, it makes sense to use corticosteroids during DTA1. If we refer to the literature, we see that corticosteroid therapy has been used in several reported cases, but its effectiveness has not been established yet [1]. Documentation of the underlying biochemical abnormality is of clinical importance in such patients since hypokalemia associated with distal renal tubular acidosis generally responds to treatment with bicarbonate alone; patients does not require potassium supplementation once potassium body stores are repleted.

CONCLUSION

In patients presenting with paraparesis secondary to hypokalemia with metabolic acidosis, evaluation of underlying cause, such as renal tubular acidosis associated with Sjogren's syndrome should be considered (dRTA1 due to SS).

Hypokalemic paralysis can also be due to renal tubular acidosis secondary to an autoimmune disorder just like in our case. One should always consider autoimmune disorders as one of the causes. Delay in the diagnosis can be avoided by meticulous search for the underlying cause of hypokalemia and evaluating the symptoms such as dry eyes, dry mouth, and fatigue.

ETHICS

Written informed consent was obtained from the patient for publication.

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AUTHORS CONTRIBUTIONS

All the authors have equally contributed to the work and also revised the same. All authors have also approved the final form.

CONFLICTS OF INTERESTS

No potential conflicts of interest.

REFERENCES

1. Francois H, Mariette X. Renal involvement in primary Sjogren syndrome. Nat Rev Nephrol. 2016;12(2):82-93. doi: 10.1038/nrneph.2015.174, PMID 26568188.

2. Talal N, Zisman E, Schur PH. Renal tubular acidosis glomerulonephritis and immunologic factors in Sjogrens syndrome. Arthritis Rheum. 1968 Dec;11(6):774-86. doi: 10.1002/art.1780110607, PMID 4178221.
3. Shearn MA, TU WH. Latent renal tubular acidosis in Sjogrens syndrome. Ann Rheum Dis. 1968 Jan;27(1):27-32. doi: 10.1136/ard.27.1.27, PMID 4170879.
4. Amaresan MS, Muthu J, Bellarmine CTJ, Cherian TJ. Renal tubular acidosis with osteodystrophy and metabolic myopathy (report of fifteen cases). J Assoc Physicians India. 1978 Apr;26(4):249-56. PMID 730698.
5. Penney MD, Oleesky DA. Renal tubular acidosis. Ann Clin Biochem. 1999 Jul;36(4):408-22. doi: 10.1177/000456329903600403, PMID 10456202.
6. Karras D, Antoniadis C, Papadakis J, Vafiadis S. Acute flaccid quadriplegia disclosing Gougerot Sjogren syndrome with renal tubular acidosis nephrocalcinosis and osteomalacia. Rev Rhum Mal Osteoartic. 1989;56(6):491-4. PMID 2740810.
7. Aerts J, Vigouroux C, Fournier P, Cariou D, Pasquier P. Osteomalacia of renal origin disclosing Gougerot Sjogren syndrome. Rev Med Interne. 1994;15(1):43-7. doi: 10.1016/s0248-8663(05)82129-0, PMID 8052753.
8. Kim YK, Song HC, Kim WY, Yoon HE, Choi YJ, KI CS. Acquired gitelman syndrome in a patient with primary Sjogren syndrome. Am J Kidney Dis. 2008 Dec;52(6):1163-7. doi: 10.1053/j.ajkd.2008.07.025, PMID 18805608.
9. Cohen EP, Bastani B, Cohen MR, Kolner S, Hemken P, Gluck SL. Absence of H(+)-ATPase in cortical collecting tubules of a patient with Sjogrens syndrome and distal renal tubular acidosis. J Am Soc Nephrol. 1992;3(2):264-71. doi: 10.1681/ASN.V32264, PMID 1391725.
10. DE Franco PE, Haragsim L, Schmitz PG, Bastani B. Absence of vacuolar H(+)-ATPase pump in the collecting duct of a patient with hypokalemic distal renal tubular acidosis and Sjogrens syndrome. J Am Soc Nephrol. 1995;6(2):295-301. doi: 10.1681/ASN.V62295, PMID 7579099.
11. Inagaki Y, Jinno Yoshida Y, Hamasaki Y, Ueki H. A novel autoantibody reactive with carbonic anhydrase in sera from patients with systemic lupus erythematosus and Sjogrens syndrome. J Dermatol Sci. 1991;2(3):147-54. doi: 10.1016/0923-1811(91)90060-b, PMID 1908698.
12. Takemoto F, Katori H, Sawa N, Hoshino J, Suwabe T, Sogawa Y. Induction of anti-carbonic anhydrase-II antibody causes renal tubular acidosis in a mouse model of Sjogrens syndrome. Nephron Physiol. 2007;106(4):63-8. doi: 10.1159/000104873, PMID 17622741.