Case Reports in Nephrology and Dialysis

Case Rep Nephrol Dial 2021;11:147–151
DOI: 10.1159/000515588
Received: November 18, 2020
Accepted: February 28, 2021
Published online: June 18, 2021

Single Case

From Hypokalemic Crisis to Sjogren's Syndrome: A Case Report and Literature Review

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Keywords
Tetraparesis · Hypokalemia · Renal tubular acidosis type 1 · Sjögren's syndrome · Corticosteroid

Abstract
Renal involvement occurs in approximately 5% of patients with Sjögren's syndrome (SS). We reported the case of a 20-year-old African woman who was received for paralysis of 4 limbs secondary to hypokalemia. The diagnosis of renal tubular acidosis type 1 complicated by hypokalemia was retained. In the etiologic research of renal tubular acidosis type 1, primary SS was retained. The patient received symptomatic treatment based on potassium chloride, sodium bicarbonate, hydration, and a low protein diet. In terms of etiological treatment, she was put on corticosteroid and hydroxychloroquine. The outcome was favorable with correction of acidosis and hypokalemia.

Introduction

Renal involvement occurs in approximately 5% of patients with Sjögren's syndrome (SS) [1]. The disorders described are very heterogeneous according to the studies [1]. Three renal lesions predominate chronic tubulointerstitial nephritis, tubulopathies, and membranoproliferative glomerulonephritis [1]. We report the case of a patient who was presented with distal renal tubular acidosis type 1 (DTA1) secondary to SS, discovered in the context of hypokalemic paralysis. We then provided an updated review of the pathophysiological mechanisms that may explain the link between DTA1 and SS.

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Case Report

A 20-year-old African woman was received at Dalal Jamm Hospital for paralysis of 4 limbs. The physical examination showed tetraparesis and arrhythmia on cardiac auscultation. The constants were for blood pressure at 120/80 mm Hg, pulse at 88 beats/min, temperature at 36.6°C, weight at 69 kg, and diuresis at 3 L. This patient had a long history of hospitalization in the neurology department for tetraparesis secondary to the hypokalemic crisis. She had no family history of kidney disease or sickle cell disease. The Schirmer test was positive. Laboratory investigations revealed on the serum ionogram: K^+: 1.4 mmol/L; Na^+: 134 mmol/L; Cl^-: 113/mmol/L, on the urine ionogram: Na^+: 250 mmol/24 h; K^+: 53 mmol/24 h; Cl^-: 254/mmol/24 h, urinary urea at 5.2 g/24, creatinuria at 139 mg/L, glycemia at 0.99 g/L, urinary osmolarity at 202.6 mmol/L, plasma osmolarity at 290.3 mmol/L, the transtubular potassium gradient (TTKG) at 5, the magnesemia at 23 mg/L, the alkaline reserves at 15.69 mmol/L, the plasma anion gap at 9.3, the urinary anion gap at 10 and the urine pH to 7.5, serum creatinine was at 7 mg/L, calcemia at 90 mg/L, phosphatemia at 25 mg/L, and calciuria at 187 mg/24 h. Abdomen X-ray showed nephrocalcinosis (Fig. 1). The diagnosis of DTA1 complicated by hypokalemia was retained. The electrocardiogram showed atrial extrasystoles. In etiologic investigations, the hemogram showed hemoglobin at 12.4 g/dL, white blood cells at 4,080/mm^3, lymphopenia at 900/mm^3, and platelets at 371,000/mm^3. TSHus was normal; C-reactive protein was negative. Electrophoresis of serum proteins showed polyclonal hypergammaglobulinemia. Anti-nuclear antibodies were positive at 380 with speckled fluorescence. The native anti-DNA antibodies were negative. The anti-SSA was positive. The accessory salivary gland biopsy showed grade 4 lymphocytic sialadenitis from Chisholm and Mason (Fig. 2). We had retained the diagnosis of primary SS because she had a score according to 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary SS at 7 (The Schirmer test positive [score = 1], labial salivary gland with focal lymphocytic sialadenitis and focus score of ≥1 foci/4 mm^2 [score = 3] and anti-SSA/Ro positive [score = 3]), and she had no exclusion criteria. Primary SS was identified as the cause of type 1 renal tubular acidosis. The patient received symptomatic treatment based on potassium chloride, sodium bicarbonate, hydration, a low protein diet, and rich in fruits and vegetables. In terms of etiological treatment, she was put on corticosteroid and hydroxychloroquine. The outcome was favorable with correction of acidosis and hypokalemia.

Discussion

The collecting tube is the site of final regulation of urinary acid excretion, and the type A intercalary cells in this segment perform the function of distal H^+ ion secretion and HCO_3 reabsorption. The secretion of H^+ is effected by the H^+ -ATPase and H^+, K^+-ATPase pumps. The H^+-ATPase pump is abundantly expressed in the membrane and the cytoplasmic vesicles of the apical pole of type A intercalary cells. The proton secretion activity is coupled with HCO_3 reabsorption activity carried out by the renal isoform of the basolateral Cl^-/HCO_3 exchanger also known as AE1. The Cl^- ion which enters the cell through the activity of the AE1 exchanger is recycled via the basolateral K^+-Cl^- cotransporter or the Cl^- ClC-kb channel. Defective type A intercalary cell function will result in hyperchloremic acidosis with 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^+, and this gradient is greater than 20 mm Hg. Hyperchloremic acidosis is associated with hypokalemia, hypercalciuria, bone disease (rickets or osteomalacia), and hypocitraturia. Hypokalemia is explained by stimulation of distal potassium

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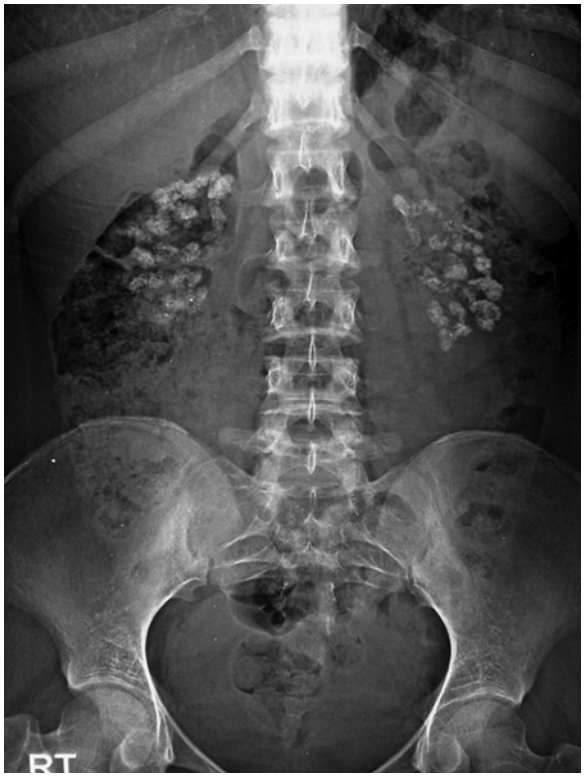

Fig. 1. Abdomen X-ray showed nephrocalcinosis.

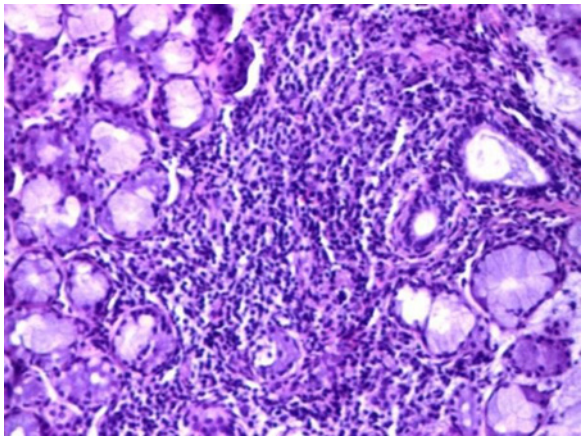

Fig. 2. The accessory salivary gland biopsy showed grade 4 lymphocytic sialadenitis from Chisholm and Mason. HE. ×10.

secretion by unreabsorbed bicarbonate and stimulation of the renin-angiotensin-aldosterone system secondary to sodium loss. Chronic acidosis stimulates proximal reabsorption of citrate (1 molecule of citrate produces 3 molecules of bicarbonate) and bone resorption; hypocitraturia, alkaline urine, and hypercalciuria will lead to nephrocalcinosis, and/or nephrolithiasis [2]. The pathogenesis of renal involvement and the pathophysiology of DTA1 during SS are still unclear [3], and probably multifactorial [4].

Kidney disease can be the consequence of tubulointerstitial infiltration of T cells, B cells, and plasma cells and, more rarely, of autoantibodies [5, 6]. The majority of patients exhibit clinical manifestations that are a direct consequence of interstitial infiltration of lymphocytes, which promotes interstitial fibrosis leading to chronic kidney disease. Tubulitis has also been

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associated with distal DTA and leads to the complete absence of H^+-ATPase in the collecting ducts [6, 7] and thiazide-sensitive NaCl cotransporter [5]. Autoantibodies have also been found against NaCl cotransporter [5] although their precise role in eliciting clinical symptoms remains to be established. 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 [8]. Autoantibodies to carbonic anhydrase enzymes have been identified in the serum of patients with primary SS [9] and seem to correlate with DTA. 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 [10]. Some of these autoantibody targets (e.g., carbonic anhydrase II and H^+-ATPase) can be found in the salivary glands and in renal intercalated cells [11]. Salivary gland injury, therefore, might cause a release of autoantigens in the kidney, which consequently become the target of both T lymphocytes and autoantibodies. Moreover, several studies have found a positive correlation between disease duration [12], hypergammaglobulinemia, and the presence of autoantibodies against SSA (Ro) or SSB (La) [13].

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 evident extra-renal signs of SS. The clinical manifestation is also characterized by repetitive episodes of hypokalemic crisis with paralysis of the limbs and which often constitutes a differential diagnosis with Westphal's disease and thyrotoxic hypokalemic paralysis.

Treatment is not codified for DTA1 secondary to SS. 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 (see above) and not to organic tubulointerstitial involvement. So 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 the effectiveness is not established yet [1].

Conclusion

The pathogenesis of renal involvement and the pathophysiology of DTA1 during SS appear to be related to immunological factors. The use of corticosteroids may be necessary in the management.

Statement of Ethics

The present case report adhered to the Declaration of Helsinki. Written informed consent for publication was obtained from the patient.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Author Contributions

Mansour Mbengue reviewed the literature and wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript. Cedric Ouanekpone revised the article critically for important intellectual content. Seynabou Diagne revised the article critically for important intellectual content and gave final approval of the version to be submitted. Abdou Niang revised the article critically for important intellectual content and gave final approval of the version to be submitted.

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