



Case Report: Renal Tubular Acidosis as The Initial Presentation of Sjogren's Syndrome

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ABSTRACT

Sjögren's syndrome (SSjP) is a chronic multisystem autoimmune disorder characterized by inflammation of the lacrimal and salivary glands, with consequent dryness of the eyes and mouth and occasional glandular enlargement, it occurs in a primary form, not associated with other autoimmune rheumatic diseases. We present the case of a 36-year-old female patient with Sjögren's syndrome whose initial clinical manifestation was extraglandular, with the kidney as the main organ affected in the form of chronic hypokalemia and distal renal tubular acidosis, which led to immunological markers being performed. for Sjögren's syndrome, the diagnosis of this autoimmune exocrinopathy allowed, achieving clinical remission and stabilization of renal function with the use of steroids.

Keywords: Sjögren's syndrome, autoimmune exocrinopathy renal tubular acidosis, hypokalemia, tubulointerstitial nephri.

INTRODUCTION

Primary Sjögren's syndrome (SSjP) is defined as an autoimmune disorder of the connective tissue with the presence of B lymphocyte infiltration in the epithelial tissues of the glands. B lymphocytes are also found in extraglandular epithelia such as the lungs, gastrointestinal tract, hepatobiliary tract, and renal epithelium.(1).

Classic clinical manifestations of SSjP (primary Sjögren's syndrome) include dryness, defined as dry eyes and mouth, which occurs in more than 90% of patients (2). Dry mouth causes pain when swallowing and tooth decay; Regarding dry eyes, it manifests itself as keratoconjunctivitis sicca that presents the following symptoms: eye pain, irritation and sensation of a foreign body in the eyes.

On the other hand, extraglandular manifestations of SSjP are found in variable forms and can affect most organic systems. Some of the known presentations include tracheobronchial sicca and interstitial pneumonia in the respiratory system, and pericarditis and pulmonary hypertension in the cardiovascular system. Other signs and symptoms may include dysphagia, arthralgia, myalgia, hypothyroidism, and skin manifestations, including nonblanching skin rashes (3). Since the condition is caused by the proliferation of B lymphocytes, the development of lymphoproliferative disorders is a major concern.

SSjP can also be secondary to other autoimmune conditions, including but not limited to systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and systemic sclerosis (scleroderma) (1). The prevalence of renal involvement in SSjP has been reported to range from approximately 10% to 30%.(4).

Kidney disease in SSjP is due to 2 different pathophysiological processes: (1) Epithelial disease with significant lymphocytic infiltration, resulting in different conditions such as tubulointerstitial nephritis (TIN), electrolyte alterations such as hypokalemia, distal renal tubular acidosis, proximal renal tubular acidosis, Fanconi syndrome, diabetes insipidus, Gitelman syndrome, nephrolithiasis and nephrocalcinosis, and (2) non-epithelial disease that can lead to glomerulopathy as a result of an immune complex-mediated process (5). (1) Epithelial disease with significant lymphocytic infiltration, resulting in different conditions such as tubulointerstitial nephritis (TIN), electrolyte alterations such as hypokalemia, distal renal tubular acidosis, proximal renal tubular acidosis, Fanconi syndrome, diabetes insipidus, Gitelman syndrome, nephrolithiasis and nephrocalcinosis, and (2) non-epithelial disease that can lead to glomerulopathy as a result of an immune complex-mediated process

CASE REPORT

A 36-year-old female patient was admitted to the nephrology service due to recurrent symptomatic severe hypokalemia, accompanied by normal anion gap metabolic acidosis and elevated creatinine. She reported marijuana abuse and toluene inhalation in her youth. She has multiple tattoos. She was hospitalized in 2021 due to weakness associated with hypokalemia, hypophosphatemia, hyperchloremia, since then with elevated creatinine, she received intravenous electrolytes with improvement and was discharged.

He was admitted with blood pressure 90/60 mmHg, with the following findings: P 1.5, Cal 8.6, Cl- 131, K+ 2.77, Na+ 145, Mg 2.24, Cr 1.90, Hb 9.9 HTO 33.3, albumin 3.34 g/dl, venous blood

gases: ph 7.23, pco2 15, hco3 8.4, anion gap 8.3, ego density 1.01, ph 6.73, proteins 25, nitrites -, leukos 5-10/field, urinary sediment with the presence of some granular casts and leukocyte casts. Proteinuria/creatinuria ratio 656.7 mg/g, urinary electrolytes Volume 9,140 ml, CLU 243, KU 116.9, NAU 319.9 mEq/24h, citrate 197 mg/24h, urinary anion gap +193.8 MEQ/L. Renal ultrasound RD 91*53*50, RI 87*46*43 both lobulated, hyperechoic cortex, decreased vascularity. Positive serologies for ANAs 1:160 +++ 1:1280 +, ANTI-SSA RO IgG 187, ANTI-SSB LA IgG 93, negative ANTI-DNA-DS and complement levels were normal.

An ultrasound-guided renal biopsy was performed, reporting 29 glomeruli with data of chronic hypoperfusion, diffuse cicatricial global and segmental sclerosis, active and chronic tubulointerstitial nephritis, focal acute tubular injury, grade II interstitial fibrosis 40-50% mild arteriolosclerosis and chronic arteriopathy. (Illustration 1). Immunofluorescence was negative (Table 1).

Sjögren's syndrome was concluded with chronic tubulointerstitial nephritis type kidney disease manifested with distal renal tubular acidosis type 1 (illustration 2). The patient received steroids and rituximab as well as a potassium citrate supplement. She presented a decrease in creatinine to 1.31 mg/dl, with normokalemia but persistent metabolic acidosis.

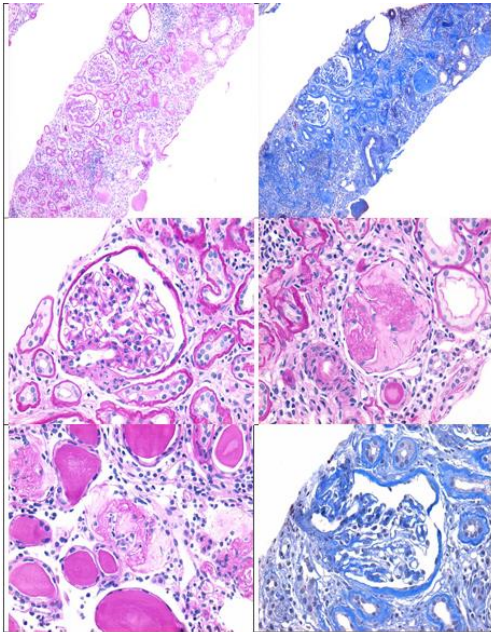


Illustration 1: Renal Biopsy Active and Chronic Tubulo-Interstitial Nephritis. O Acute Focal Tubular Lesion with Moderate Regenerative Changes of The Epithelium. O Chronic Glomerular Hypoperfusion With Diffuse Global and Segmental Sclerosis. O Interstitial Fibrosis Grade Ii (40-50%). Or Mild Arteriolosclerosis. O Chronic Arteriopathy

Table 1: Direct Immunofluorescence Study in Dewaxed Tissue

Immunoreact	Result
IgG	Positive with pattern linear in the membranes
IgA	Negative
IgM	Negative
C1q	Negative

C3c	Positive in arteriolar walls
C4c	Negative
Fibrinogen	Negative
Albumin	Positive with pattern linear in the membranes basal glomerular
Kappa	Negative
Lambda	Negative

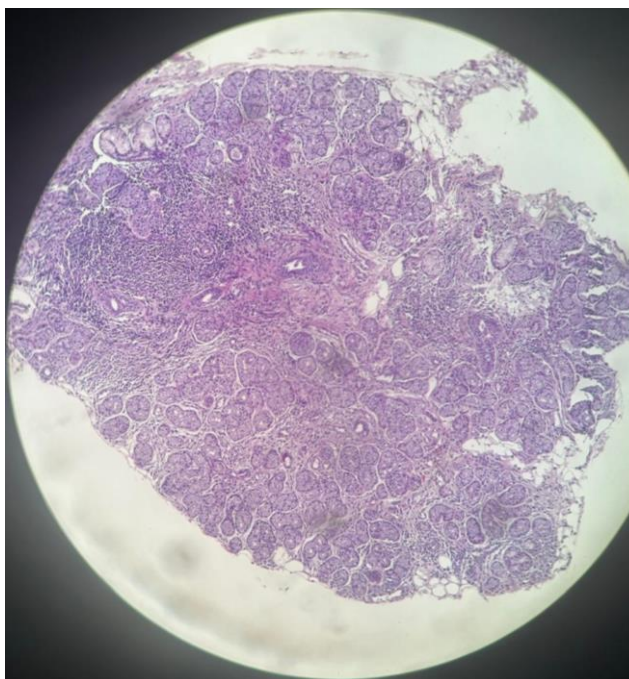


Illustration 1: Lip biopsy: group of minor salivary glands surrounded by moderate chronic inflammation. Presence of chronic lymphocytic infiltrates (so-called lymphocytic foci), composed mainly of T and B lymphocytes with some other mononuclear cells

DISCUSSION

The diagnostic approach to refractory hypokalemia must consider the suspicion of tubular disease. ATR is a clinical syndrome characterized by normal anion gap metabolic acidosis, within the spectrum of ATR it is classified as: proximal type II RTA, distal type I RTA, mixed type III RTA and hyperkalemic type IV RTA.

The test with furosemide consists of the administration of 2 mg/kg/dose, measuring urinary pH for 3 hours. If the pH reaches values <5.8, it means that the distal acidification mechanisms are intact. Furosemide inhibits the reabsorption of sodium chloride in the loop of Henle and allows greater supply of sodium and chloride to the distal tubule. If the distal mechanisms are intact, sodium is reabsorbed and H is eliminated.

Our patient presents the association of metabolic acidosis, kidney disease and refractory hypokalemia, for which ATR type I is integrated. This type of metabolic acidosis is characterized by a decrease in the distal reabsorption of HCO_3^- and urinary excretion of hydrogen ions, resulting in a defect in the distal acidification.

In a patient with distal RTA and tubulitis in the kidney biopsy, immunocytochemical analysis showed a complete absence of the H-ATPase pump in the intercalated cells in the collecting ducts, which is largely responsible for the distal secretion of protons (6). In some patients with PSjD who have hypokalemia without TKA, the primary defect is thought to be urinary sodium loss due to tubular injury (7). Increased sodium delivery to the potassium secretory site in the collecting ducts and increased aldosterone release due to volume depletion lead to urinary potassium loss and potentially severe hypokalemia.

Autoantibodies may be the cause of acid-base and electrolyte abnormalities in some patients with SjD. High titers of an autoantibody directed against carbonic anhydrase II have been reported in some patients with PSjD and distal RTA; Inhibition of this enzyme would result in the generation within the cell of fewer hydrogen ions available for secretion (8). In a patient with SjD and hypokalemia due to urinary sodium loss, a circulating autoantibody directed against the sodium chloride cotransporter was identified.

Clinically, a symptomatological sequence is evident that begins with metabolic acidosis, hypokalemia, muscle weakness, hyporeflexia and paralysis. Analytically, it is characterized by severe acidosis, decreased HCO_3^- , alkaline urinary pH (greater than 7), fractional excretion of bicarbonate (EFHCO_3^-) less than 3% and nephrocalcinosis – nephrolithiasis.

Chronic kidney disease (CKD) due to tubulointerstitial nephritis is the most common renal manifestation of SSjP (9). The clinical presentation of PSjD-associated tubulointerstitial nephritis may be subtle, asymptomatic, and detectable only by laboratory tests. Clinical manifestations include CKD of varying severity, a relatively benign urinalysis, and frequently abnormalities in tubular function, such as distal renal tubular acidosis (RTA) (type 1), Fanconi syndrome, arginine vasopressin resistance, and hypokalemia.

Regarding etiology, they can be primary (Sjögren's disease, rheumatoid arthritis, systemic lupus erythematosus) or secondary (hypercalciuria, drugs, amphotericin, lithium, ifosfamide, sickle cell anemia, obstruction, kidney transplant). The association of clinical presentation, immunological markers and pathological evidence compatible with Sjögren's syndrome at the glandular and extraglandular level is needed.

Treatment is carried out with correction of bicarbonate level slowly, progressively and with continuous monitoring of calcium level and potassium level, in addition to calcium supplements in association with primary treatment for SSjP.

CONCLUSION

Type I RTA is a rare disorder that affects the renal tubules and is fundamentally characterized by metabolic acidosis with a normal anion gap, hydroelectrolyte disorders (refractory hypokalemia) and inability to acidify urine. Its association with SS has been widely described in the scientific literature, constituting one of the most frequent forms of renal clinical manifestation. Basic laboratory studies that allow us to suspect the presence of type I TKA are simple to perform and are available in most health centers; Therefore, in an appropriate clinical context, the presence of certain alterations (hydroelectrolytic and metabolic) suggestive of ATR requires ruling out the presence of autoimmune disorders, mainly SS. Early diagnostic suspicion, especially in the presence of infrequent manifestations, allows for a targeted physical

examination and the request of complementary studies that contribute to the definitive diagnosis of the disease. Early treatment of type I TKA associated with SS, especially the correction of the different metabolic alterations, prevents the development of complications, which improves the quality of life of patients.

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