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Distal Renal Tubular Acidosis and Diabetes Insipidus Leading to the Diagnosis Of Sjögren's Syndrome

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INTRODUCTION

Sjögren's syndrome is a chronic inflammatory disease characterized by the infiltration and progressive destruction of salivary and lacrimal glands. A common presentation involves the complaints of dry eyes and dry mouth, known as the "sicca complex." Extra-glandular involvement is not uncommon, and is known to involve the lungs, vascular and peripheral nervous system, and kidney.¹ The reported renal involvement ranges broadly from 2 – 67%, and is variably defined: the most commonly reported renal pathology is an a tubulo- interstitial nephritis resulting in tubular dysfunction and immune-mediated glomerular disease; however distal renal tubular acidosis (RTA) in particular can be present in 20-30% of cases.^{2,3} Although there have been case reports of patients with Sjögren's syndrome presenting with distal RTA during the course of the disease, to our knowledge, a diagnosis of Sjögren's syndrome made solely on the basis of renal manifestations without any overt physical findings of the disease has not been documented.

CASE PRESENTATION

A 37 year old female presented to another hospital with progressive fatigue over the course of three months, and debilitating weakness, nausea, and non-bloody non-bilious vomiting over the course of one week. Her review of systems was negative except for mild depression after losing her job, for which she denied use of any psychiatric medications. She was also eating a healthy and variable diet with no change in appetite and no weight loss. She did not have musculoskeletal, cutaneous, or pulmonary symptoms. Her past medical history included a deep vein thrombosis and pulmonary embolism five years prior following an airplane ride. Family history was significant only for maternal type 2 diabetes mellitus.

Initial vital signs showed episodes of sinus bradycardia responsive to atropine, and were otherwise within normal limits. Physical examination showed profound bilateral upper and lower extremity weakness, decreased reflexes in all muscle groups, and absent Babinski's sign. Laboratory studies on admission showed the following: potassium 1.1 mEq/L, sodium 132 mEq/L, chloride 116 mEq/L, bicarbonate of 9 mg/L, creatinine 2.6 mg/L, pH 7.07. A urine drug screen was negative. Electrocardiogram showed sinus bradycardia, flattened T waves, and U waves (**Figure 1**). On the second day of admission, the

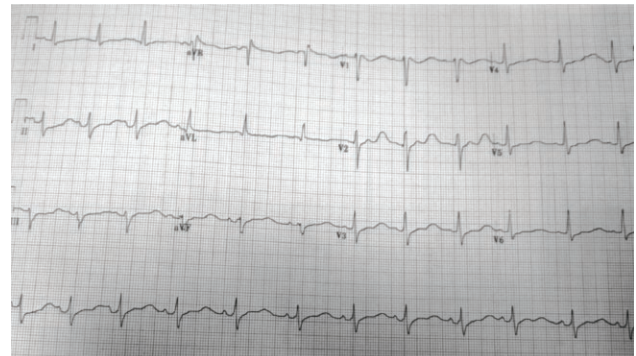


Figure 1. Electrocardiogram shows flattened T waves and U waves

sodium level increased to 159 mEq/L. Her mental status worsened, and she became obtunded. She was intubated and mechanically ventilated.

Aggressive repletion of her potassium was initiated along with fluid resuscitation with bicarbonate drip, lactated ringers, and normal saline for her severe acidosis. A therapeutic dose of low molecular weight heparin was initiated due to incidentally found lower extremity deep vein thrombosis on duplex ultrasound. Due to an abnormal neurologic exam, a CT scan of the head was performed which showed a pontine hemorrhage with localized mass effect. She was subsequently transferred to Thomas Jefferson University Hospital for management of pontine hemorrhage and evolving electrolyte abnormalities.

On further questioning of family members, the patient had several months of increasing polyuria and polydipsia, drinking 2-3 gallons of water a day and urinating every two hours, including during the night. Further testing revealed the following labs: serum osmolality 345 mOsm/kg, urine osmolality 274 mOsm/kg, urine sodium 57 mEq/L, urine potassium 6 mEq/L, urine chloride 49 mEq/L, urine creatinine 19.7 mg/dL, urine pH 7.5. Renal ultrasound showed bilateral increased cortical echogenicity, suggestive of renal parenchymal disease.

INTERPRETATION AND DIAGNOSIS

This patient had a non-anion gap metabolic acidosis, and a positive urine anion gap. Her urine pH was inappropriately elevated. These values suggested a distal type renal tubular acidosis. She was hypokalemic with an elevated transtubular

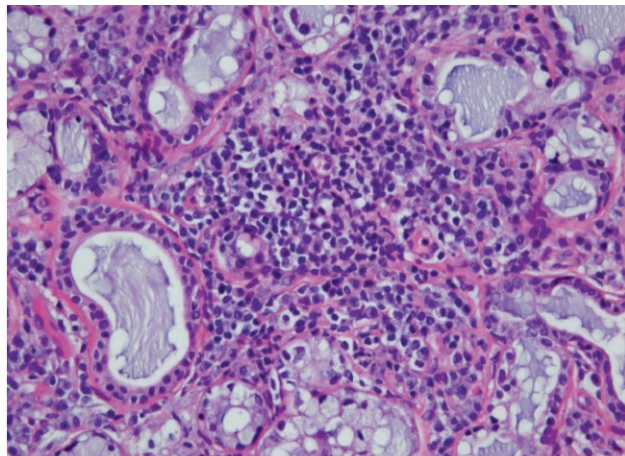


Figure 2. Buccal biopsy section showing lymphocytic infiltrate, 40x magnification

potassium gradient, suggesting renal losses as the cause for her hypokalemia. The persistent hypernatremia, along with inappropriately low urine osmolality correlate with diabetes insipidus, which was likely compensated for by polydipsia in the outpatient setting.

This combination of renal insufficiency, distal type renal tubular acidosis and diabetes insipidus was suggestive of tubulointerstitial disease. As there were no toxic drug exposures, and no family history of renal disease, serologic testing for autoimmune conditions was performed. High titers of anti-nuclear, anti-SSa and anti-SSb antibodies were found, suspicious for primary Sjögren's syndrome. A biopsy of the salivary glands of the lip showed focal lymphocytic sialadenitis (**Figures 2 and 3**), confirming the diagnosis of Sjögren's syndrome.

Treatment with corticosteroids for Sjögren's disease was initiated. Amiloride was initiated for treatment of hypokalemia in addition to potassium supplements. Her electrolyte levels normalized with these treatments. The patient had a neurologic exam consistent with locked-in syndrome and her neurologic prognosis was poor. Renal biopsy was not performed due to improvement with medical therapy, suggesting that there would be no change in management with biopsy.

DISCUSSION

This case is unique in that the diagnosis of Sjögren's syndrome was made solely on the basis of renal manifestations without any overt physical findings of the disease. Sjögren's syndrome is an autoimmune disorder which is characterized by polyclonal B-cell activation as well as lymphocytic infiltration of the exocrine glands, resulting in keratoconjunctivitis and/or xerostomia.² According to a biopsy proven study, Sjögren's syndrome can induce a defect in the proton secretion in intercalated cells due to a lack of H⁺ ATPase.⁴ In addition, tubulointerstitial nephritis

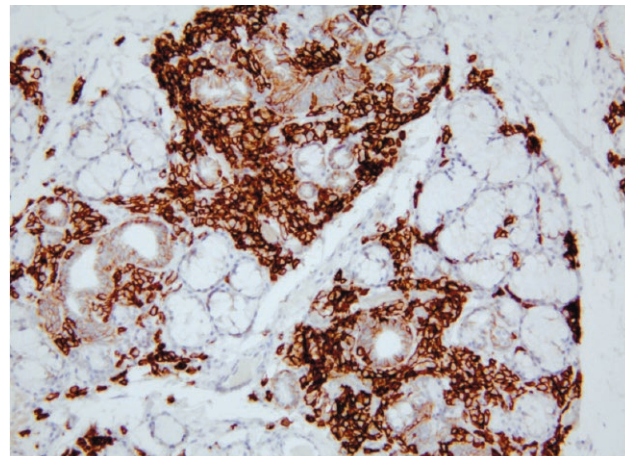


Figure 3. Buccal biopsy with CD138 stain, showing an infiltrate of plasma cells

can lead to defects in the urine concentrating capacity, which may cause partial nephrogenic diabetes insipidus.⁵ Renal manifestations of Sjögren's syndrome include acute or chronic tubulointerstitial nephritis, immune-mediated glomerular disease and less commonly, cryoglobulinemia, nephrocalcinosis and nephrogenic diabetes insipidus.⁶

In patients with interstitial nephritis due to Sjögren's disease, treatment modalities reported include steroids, steroids with cyclophosphamide, and steroids with azathioprine. The data available is scant, precluding an analysis of the relative benefits of each modality.⁷ In our patient, corticosteroids without other adjunctive immunosuppressive agents was used, with an adequate response.

In conclusion, in a patient with evidence of tubulointerstitial nephritis without underlying renal disease or other etiology, it is important to recognize Sjögren's syndrome as a possible

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