CLINICAL VIGNETTE

35-Year-Old Female with Sjögren Syndrome and Chronic Kidney Disease

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Case Summary

A 35-year-old female presented to rheumatology clinic to establish care for Sjögren syndrome. She had history of medullary sponge kidney and polycystic ovary syndrome (PCOS), with recurrent nephrolithiasis requiring lithotripsy and open surgical interventions. She was followed by an outside nephrologist. Her first symptomatic kidney stone occurred four years prior to presentation. She had a history of renal tubular acidosis (RTA) type 1 felt secondary to medullary sponge kidney. The medullary sponge kidney and RTA were diagnosed about three and a half years prior to presentation. She had resulting low potassium levels, which she "could not get up", even with significant potassium supplementation. She had associated chronic kidney disease (CKD) with baseline creatinine around 1.4 mg/dL (with creatinine up to 1.6 mg/dL at times). She had never had a kidney biopsy.

She had been diagnosed with Sjögren syndrome by an outside rheumatologist two years prior to presentation, based on sicca symptoms and positive serologies for Sjögren syndrome (including rheumatoid factor, SS-A, and SS-B antibodies). She also had evidence of systemic inflammation, with erythrocyte sedimentation rate (ESR) of 92 mm/hr. She described dental problems for 18 years, with significant dental caries and multiple crowns and implants. She also had associated arthralgias in her hips, knees, and ankles. She had been started on hydroxychloroquine and cevimeline by her rheumatologist, six months prior to presentation. She had recently started cyclosporine eye drops and artificial tears that she used twice per day.

Vital signs were normal. Exam was notable for mild dryness of the conjunctivae and oropharynx, including decreased salivary pool. Cardiopulmonary and musculoskeletal exams were unremarkable.

Further work up at our medical center demonstrated a positive anti-nuclear antibody in high titer (>=1:1280), with borderline double stranded DNA antibody. She had no evidence of proteinuria on urinalysis, but did have significant pyuria (219 WBCs/μL). She was referred to nephrology at our medical center for a second opinion. Due to concern for possible Sjögren related interstitial nephritis as a component for her CKD, she was sent for kidney biopsy. Biopsy demonstrated chronic active interstitial nephritis with minimal interstitial fibrosis and tubular atrophy. The interstitial inflammation was composed mostly of plasma cells, with fewer lymphocytes and several eosinophils. There were scattered immune complex deposits within tubular basement membranes seen on electron microscopy that stained for IgG by immunofluorescence. There was no evidence of immune complex deposition within the glomeruli, and no glomerulonephritis present. The overall findings were felt related to Sjögren syndrome more than medication related injury.

Discussion

Sjögren syndrome is a systemic autoimmune condition most often characterized by sicca symptoms (dryness of the eyes, mouth, and other mucus membranes). Typically, there is a lymphocytic and plasmacytic infiltration of the salivary, lacrimal, and parotid glands. Non-exocrine manifestations can also occur, including involvement of integumentary, musculoskeletal, pulmonary, cardiovascular, gastrointestinal, nervous, hematologic, and urogenital systems. The prevalence of renal involvement in Sjögren syndrome has varied widely across studies, partly due to differences in the definition of renal involvement and the presence of sub-clinical disease. In one study of 60 patients with primary Sjögren syndrome (pSS), 27 percent had evidence of tubular and/or glomerular involvement.[1]

The most frequent renal manifestation of pSS is chronic tubulointerstitial nephritis (TIN),[2] characterized by an interstitial infiltrate that damages the tubules.[1] Chronic disease can lead to interstitial fibrosis and tubular atrophy. The interstitial nephritis is typically associated with a relatively bland urinalysis and mild creatinine elevation (though this can vary), in addition to tubular dysfunction including type 1 distal RTA (less commonly type 2), hypokalemia, and nephrogenic diabetes insipidus (renal resistance to the effects of antidiuretic hormone).[3-5]

There is limited data to dictate optimal treatment of interstitial nephritis in Sjögren syndrome. However, it is generally felt appropriate to give a trial of systemic steroids in the case of severe, active TIN (e.g. significant tubulointerstitial inflammation on biopsy, with mild to moderate interstitial fibrosis).[6] There is anecdotal evidence to support improvement or stabilization of renal function. Prednisone is typically started at doses of 1 mg/kg/day (up to 60 mg) until improvement or stabilization of kidney function, followed by taper over 6-8 weeks. If patients are unable to taper off prednisone due to relapse of disease (manifested as worsening renal function or pyuria), then

steroid sparing agents such as azathioprine or mycophenolate mofetil are often used for maintenance therapy.[6-8]

Our Patient

We initiated treatment with prednisone 60 mg/day. Prior to starting prednisone her creatinine was 1.5 mg/dL, with on-going pyuria (126 white blood cells per microliter). Over the course of 2 weeks she had resulting improvement in her creatinine to 1.3 mg/dL and pyuria to 20-40 white blood cells per microliter. However, with taper of prednisone down to 20 mg/day creatinine rose back up to 1.6 mg/dL, with >= 60 white blood cells per microliter. Azathioprine was added, with gradual uptitration to 1.5 mg/kg/day. Prednisone was tapered off. Azathioprine monotherapy led to improvement in creatinine (average 1.2 mg/dL) and pyuria (average 6-10 white blood cells per microliter), however she developed progressive leukopenia and rising liver enzymes.

She was transitioned to mychophenolate mofetil at a dose of 1,000 mg twice per day, which has maintained pyuria at a low level (currently 6-10 white blood cells per microliter). Her creatinine was initially maintained at 1.2 mg/dL, however on recent testing has risen to 1.5 mg/dL. This may represent normal variation unrelated to her underlying inflammatory condition. However, if this persists consideration will be given to advancing mycophenolate dose further (up to 1,500 mg twice per day), or perhaps selecting an alternate steroid sparing agent.

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