CASE REPORT

Isolated end-stage renal disease in Sjögren’s syndrome due to immune complex mediated glomerulonephritis

Shashank Agarwal1,*, Jaishvi Eapen1, Ming Wu2, Bruce Garner3 and Adib Alhaddad4

1Department of Internal Medicine, NYU Langone Health, Brooklyn, NY, USA, 2Department of Pathology, NYU Langone Health, NY, USA, 3Department of Rheumatology, NYU Langone Health, Brooklyn, NY, USA, and 4Department of Nephrology, NYU Langone Health, Brooklyn, NY, USA

*Correspondence address. 150 55th Street, Station 2-03, Brooklyn, NY 11220, USA. Tel: +1-929-257-5243; Fax: +1-347-377-3780; E-mail: Shashank.agarwal@nyumc.org

Abstract

Renal involvement is an uncommon extra-glandular manifestation in Sjögren’s syndrome (SS). We present the case of a young male who presented with nephrotic range proteinuria and advanced irreversible renal disease, with positive anti-Ro antibody (Ab) and antineutrophil cytoplasmic antibody (ANCA) with myeloperoxidase (MPO) specificity. He was initially treated with steroids for suspected ANCA vasculitis but treatment was discontinued as there was no response and renal biopsy revealed interstitial lymphocytic infiltrates, advanced glomerular disease with immune complex mediated glomerulonephritis more suspicious for SS. SS usually affects exocrine glands and patients rarely have renal involvement in which cases it is commonly tubulo-interstitial nephritis. This report describes a rare case of anti-Ro Ab and MPO–ANCA positive patient with advanced irreversible renal disease due to immune-complex mediated glomerulonephritis felt to be due to SS and without any classic sicca symptoms.

INTRODUCTION

Sjögren syndrome (SS) described by Henrik Sjögren in 1933, is a chronic inflammatory disorder characterized by lymphoplasmacytic infiltration of the exocrine glands whose most common manifestation is sicca syndrome [1]. Involvement in SS is not restricted to the exocrine glands, and almost a third of patients present with extra-glandular involvement. Renal involvement in SS has been reported to occur in 10-30% of the patients [2]. The most frequent form of nephropathy in SS is tubulo-interstitial nephritis (TIN), as a result of lymphocytic infiltration of the interstitium surrounding the renal tubules. Glomerular involvement is less frequently detected in patients with SS, usually in the form of membranoproliferative glomerulonephritis most commonly, secondary to cryoglobulinaemia [3]. Here we describe a case of SS in a young patient who presented with advanced irreversible renal disease due to immune-complex mediated glomerulonephritis, on laboratory workup found to have anti-Ro Ab and MPO–ANCA positive felt to be due to SS and without any classic sicca symptoms.

CASE

A 27-year-old Chinese male presented to our institution with 1 month of generalized weakness, polydipsia and polyuria. He stated that 3 years ago he was found to have proteinuria on routine
laboratory testing but had no subsequent follow up. He denied any history of fever, headaches, chest pain, shortness of breath, abdominal pain, diarrhea, rashes, dysuria, joint and muscular pains. He was studying engineering and denied any exposure to toxins. There were no significant findings on physical exam, no parotid swelling and Schirmer’s test was negative. Significant laboratory findings were proteinuria (>3 gm/24h), microscopic hematuria, electrolyte abnormalities (hyperkalemia, without T wave changes on EKG and hyperchloremia), elevated BUN (84 mg/dl) and creatinine (Cr 6.9 mg/dl) with an estimated glomerular filtration rate (eGFR) of 10 ml/min/1.73 m². Glycosylated hemoglobin was normal (6.1) and his blood glucose levels were <160 consistently during his hospital stay without requiring any insulin administration. Double-stranded DNA (ds-DNA), smit antibody, proteinase-3 (PR-3) antibody and hepatitis C virus antibody were negative. C3 and C4 complement levels were normal. Pertinent positive laboratory tests were anti-nuclear antibody (ANA) with a speckled pattern, positive anti-Ro Ab and perinuclear antineutrophil cytoplasmic autoantibody (ANCA) with myeloperoxidase (MPO) specificity, MPO-ANCA titer was 2.5 (laboratory reference normal value is <3). Based on a high degree of suspicion for ANCA vasculitis, patient was initially treated with pulse steroids without any improvement. Light microscopy of renal biopsy showed interstitial lymphocyte infiltrates but the glomeruli were predominantly sclerotic with only a few patent showing prominent glomerular basement membrane and mesangial expansion, moderate interstitial fibrosis associated with tubular atrophy (Fig. 1). Immunofluorescence microscopy showed irregular capillary loop, and mesangial staining for IgM, C3, C4, C1q, kappa and lambda (Fig. 2). Based upon the results of the renal biopsy and a lack of response to steroids, they were discontinued and hemodialysis initiated. The patient’s symptoms have resolved and he is currently awaiting evaluation for renal transplant.

DISCUSSION
We have described the case of a patient presenting with nephrotic range proteinuria and chronic renal insufficiency with laboratory and renal biopsy findings suggestive of SS. In order to reach this conclusion, we have attempted to carefully exclude other systemic autoimmune disease, such as systemic lupus erythematosus (SLE) and ANCA vasculitis. Our patient did not have involvement of any other organ system—no arthralgia or myalgia (suggestive of musculoskeletal involvement), no signs and symptoms of either respiratory (pleurisy—normal CXR) or cardiac (pericarditis—normal EKG) involvement, unremarkable hematological panel (normal RBC, WBC and platelets) suggestive of any hematological involvement, no rashes, purpura or urticaria (suggestive of skin involvement) or any neuropsychiatric symptoms (such as seizures or psychosis). With the lack of involvement of any other organ system, and with a negative ds-DNA and renal biopsy without any features of glomerulonephritis seen in lupus [4], our suspicion for SLE was very low. Though there have been reports of anti-dsDNA negative and anti-Ro positive lupus nephritis [5], we believe our patient did not have lupus as his ANA pattern was speckled which is less commonly seen with lupus and the renal biopsy did not resemble any of the ASN classification of glomerulonephritis seen in lupus [4]. With the lack of immunofluorescence staining on renal biopsy and no improvement in renal function after administration of steroids, suspicion for ANCA vasculitis was less likely.

We believe our patient had Sjögren’s because he had positive ANA with a speckled pattern, positive anti-Ro Ab and MPO-ANCA with renal biopsy showing interstitial lymphocyte infiltrates. Renal symptoms in SS usually present in patients >50 years age [6, 7], but studies with Chinese patient cohort with renal symptoms were aged less than or equal to 40 years [8] and our patient was 27 years old Chinese male which aligns with previous published data. Our patient had positive MPO-ANCA and its presence has been correlated with extra- and intra-glandular manifestations in SS [9] which supports the renal involvement in our patient. Renal disease in SS is due to 2 distinct pathophysiological processes: (i) epithelial disease with significant lymphocytic infiltration, resulting in different conditions like TIN, electrolyte disturbances like hypokalemia, distal renal tubular acidosis, proximal renal tubular acidosis, Fanconi syndrome, diabetes insipidus, Gitelman syndrome, nephrolithiasis and nephrocalcinosis; and (ii) non-epithelial disease that can lead to glomerulopathy as a result of an immune complex-mediated process [3, 10]. In a study by Andreas et al., renal involvement occurred in 4.9% of 715 patients with Sjögren’s syndrome, with glomerular involvement occurring more frequently than tubulo-interstitial disease; 37% had interstitial nephritis alone, 49% had glomerulonephritis alone, and 14% had both. The prognosis appears to be worse in patients with predominantly glomerular involvement, with lower

Figure 1: Periodic acid-Schiff (PAS) stain light microscopy demonstrating glomerulus with mesangial expansion, interstitial inflammation and fibrosis

Figure 2: Immunofluorescence of the kidney biopsy. Here, granular staining for C1q in mesangial and irregular capillary wall can be seen.
survival rates and higher incidence of lymphoma, compared with patients with predominantly tubulo-interstitial involvement [6]. Renal biopsy in our patient revealed interstitial lymphocyte infiltrates with globally sclerotic nephrons and moderate chronic interstitial inflammation with evidence of immune complex disease, suggestive of Sjögren’s disease resulting from immune complex mediated glomerulonephritis.

**CONCLUSION**

We have described a rare case of anti-Ro Ab and MPO-ANCA positive, immune complex mediated glomerulonephritis felt to be due to Sjögren’s Disease in a patient without any classical sicca symptoms. While the patient was ANA and ANCA positive, his renal disease was less likely a result of an SLE or ANCA vasculitis. Although Sjögren’s disease usually affects the kidney with tubulo-interstitial involvement, one must be aware of the possibility of this rare type of presentation.

**CONFLICT OF INTEREST STATEMENT**

None declared.

**REFERENCES**