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*Case Report*

# Primary Sjogren's Syndrome with Involvement of Both Tubulointerstitial and Glomerulo-Nephritis - a Rare Case Report

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## ABSTRACT

Sjogren's syndrome is a rare autoimmune disease characterised by keratoconjunctivitis sicca due to autoimmune destruction of exocrine glands. Tubulointerstitial nephritis is the most common renal manifestation while glomerulonephritis is rare in Sjogren's syndrome. Here we report a case of primary Sjogren's (pSS) who presented as acute renal failure due to mesangial proliferative glomerulonephritis in addition to the coexistent tubulointerstitial nephritis.

***Key words:*** Autoimmune disease, exocrine glands, Tubulointerstitial nephritis, glomerulonephritis.

## INTRODUCTION

Sjogren's syndrome is a systemic autoimmune connective tissue disease characterised by lymphocytic infiltration of the exocrine glands leading to xeropthalmia and xerostomia. [1] Sjogren syndrome can be either primary in the absence of other connective tissue disease or secondary to autoimmune diseases like rheumatoid arthritis, systemic lupus erythematosus, polymyositis and systemic sclerosis. Although the hallmark clinical features include dry eyes and dry mouth, three-quarters of patients with primary Sjögren's syndrome manifest symptoms or signs of extraglandular disease. [2] Of the extraglandular manifestations, renal involvement in primary sjogren is usually rare, affecting <10% of patients. [2]

The most common renal involvement in pSS is tubulointerstitial nephritis (TIN) manifesting as polyuria, renal colic and tubular proteinuria. TIN is usually indolent, occasionally results in mild to moderate renal dysfunction. [3] Glomerulonephritis is less frequently detected, usually takes the form of membranoproliferative or mesangio-proliferative secondary to cryoglobulinaemia. [4] Here we report a case of primary Sjogren's who presented as acute renal failure due to mesangial proliferative glomerulonephritis in addition to the presence of tubulointerstitial nephritis.

## CASE HISTORY

A 40 year old female, known hypothyroid on thyroxine supplementation since 5 years, presented with acute onset of oliguria, swelling of both the legs and progressive weakness of all the 4 limbs of 3 days duration. History of polyarthralgia and

dryness of mouth were present for the past 6 months. No history of any skin rashes/ oral ulcers/ photosensitivity/ Raynaud's phenomenon. No history of fever/ diarrhoea/ vomiting/abdominal pain/ breathlessness/ chest pain/ palpitation. No history of any other drug intake. Not a known diabetic, hypertensive, cardiac or renal disease. On examination, she was moderately built and pale with bilateral pitting pedal oedema. Vital signs were stable. Systemic examination showed normal cardiovascular and respiratory systems. Per abdominal examination was normal. Neurological examination showed quadriparesis with the muscle power of 3/5 in both upper and lower limbs with normal superficial and deep tendon reflexes. Sensory system examination and cranial nerve examination was normal.

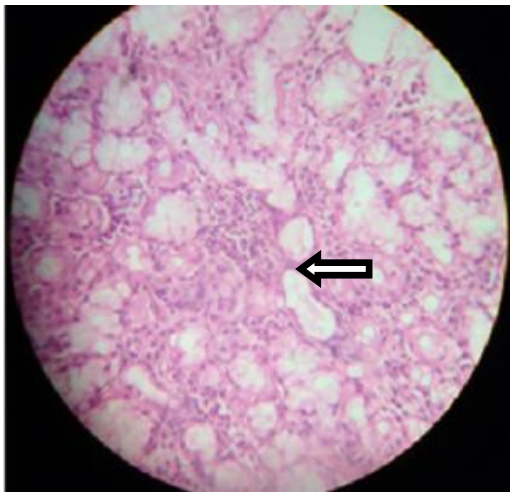

**Figure 1: Histopathological section of minor salivary glands showing multiple lymphocytic foci with normal acini and ducts.**

Investigations showed anaemia (Hb-9.8gm %) with normal WBC & platelet counts, elevated acute phase reactants (ESR-40mm/hr; CRP-12mg/L), raised renal parameters (blood urea-68mg/dl; serum creatinine-2.8mg/dl), and hypokalaemia (Na+-141meq/l, K+-2.2meq/l). Serum calcium 9.7mg/dl; phosphorus 2.8mg/dl; creatine kinase 45 IU/l; lactate dehydrogenase 120 IU/l. Thyroid function test was normal. Urine analysis showed output of 350ml/day, albuminuria (2+), nil deposits and Protein creatinine ratio of 5.4. Arterial blood gas analysis revealed non anion gap metabolic acidosis (pH 7.28, pCo2 -36mmHg, HCo3-17mEq/l). Further analysis of urine showed pH of 6.9, specific gravity 1.010, osmolality 135mosm/l, $Na^+$ 36mEq/l, $K^+$ 14 mEq/l, and Cl- 37mEq/l and urine anion gap +13. Ultrasound abdomen was normal. She was diagnosed to have acute renal failure and hypokalemic paralysis due to distal renal tubular acidosis (dRTA).

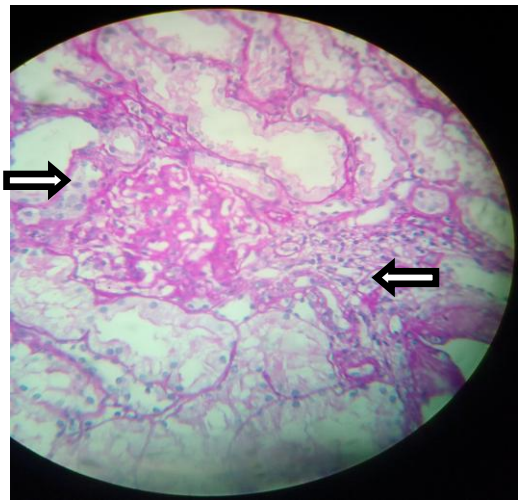

**Figure 2: Histopathological study of renal biopsy showing mesangial proliferative glomerulonephritis with tubulointerstitial inflammation**

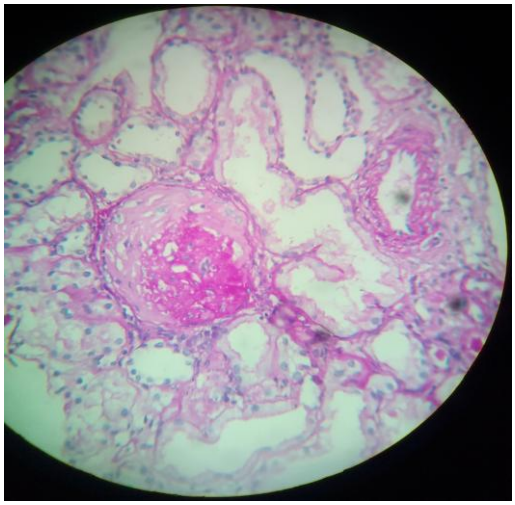

**Figure 3: HPE of renal biopsy showing global sclerosis of glomerulus.**

Patient was treated with hemodialysis along with potassium supplementation, correction of metabolic acidosis and other supportive measures. Following treatment, her muscle power improved and hypokalemia got corrected

(Rpt K+ 3.8) but continued to have proteinuria (urine PCR of 5.7 and 24 hrs urine protein of 780mg). Immunological work up showed Rheumatoid factor of 32 IU/l, speckled pattern in ANA (IIF) and positive anti-SSA, anti-Ro 52 antibodies in ANA (Immunoblot) with low C4 and normal C3 complement levels (C3-1.3mg/dl; C4-0.2 mg/dl) and positive serum cryoglobulins. Viral serology for HBV, HCV and HIV were negative. Schirmer's test was positive (<5mm) in both the eyes. Lip biopsy revealed features of multiple lymphocytic foci with normal appearing minor salivary glands, suggestive of Sjogren's syndrome (figure 1). In view of persistent proteinuria, renal biopsy was done which showed increase in mesangial cellularity and mesangial matrix along with interstitial inflammation; Few glomeruli were globally sclerotic; IgG (2+), C3 (2+) over mesangium suggestive of mesangial proliferative glomerulonephritis with tubulointerstitial inflammation (figure 2,3). Patient was treated with corticosteroids and immunosuppression with rituximab therapy. Following treatment with corticosteroids and rituximab, patient responded well with significant improvement in sicca symptoms and proteinuria. Repeat serum cryoglobulins done after six months of therapy was negative.

## DISCUSSION

The most common presentation of renal involvement in primary Sjogren's syndrome is Tubulointerstitial nephritis. [5] There are many case reports of Primary Sjogren's syndrome presenting as hypokalemic paralysis due to tubulointerstitial nephritis. [6] Rao et al 2006 studied 31 cases of hypokalemic periodic paralysis of which 3 patients had Sjogren syndrome. [7] Hypokalemia due to distal RTA as a presenting manifestation has been reported in < 2% cases of pSS. [8] Glomerulonephritis associated with primary Sjogren's syndrome is a rare occurrence that tends to develop late in the course of the disease. [3] A clinicopathological study of renal involvement in Sjogren's syndrome shows a wide variety of pathology including, membrano-proliferative glomerulonephritis, mesangial proliferative glomerulonephritis, focal segmental glomerulosclerosis and tubulointerstitial nephritis. [4] In most of these patients, pathogenesis of glomerulonephritis was attributed to deposition of immune complexes formed by cryoglobulins; however, glomerular disease may also occur in the absence of circulating cryoglobulins. [9]

Our case presented with acute renal failure and quadriparesis secondary to hypokalemia, due to tubulointerstitial nephritis of Sjogren's syndrome. Treatment with potassium supplementation and hemodialysis corrected hypokalemia and renal failure. Despite treatment, patient had persistent and significant proteinuria which necessitated renal biopsy. Biopsy revealed evidence of mesangial proliferative glomerulonephritis along with features of tubulointerstitial inflammation. Mesangial proliferative glomerulonephritis was probably due to associated cryoglobulinemia. Prevalence of Cryoglobulins were detected in about16% of pSS patients. [10]

Acute renal failure as a presenting manifestation as reported in our patient, is rare in pSS, though mild renal insufficiency due to tubulointerstitial nephritis can occur. A similar case of acute renal failure due to mesangial proliferative glomerulonephritis was reported in a pregnant woman with primary Sjogren's syndrome. [8] In our patient, treatment with corticosteroids and rituximab resulted in renal remission with improvement in sicca symptoms. Study by Meijer et al, showed that rituximab was effective and safe treatment strategy for patients with primary SS. [11] Cacoub et al. have reviewed 57 cases published on mixed cryoglobulinemia treated with rituximab and observed a favourable clinical response in 83% patients with compromised renal function. [12]

## CONCLUSION

Our case report showed the coexistence of both tubulointerstitial nephritis and glomerulonephritis in Primary Sjogren's syndrome, which has not been previously reported in the literature. Therefore, in patients with Sjogren's syndrome, presenting with renal involvement and significant proteinuria, though infrequent, the presence of glomerulonephritis should be evaluated especially in the presence of circulating cryoglobulins.

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