Renal Involvement and Followup of 130 Patients with Primary Sjögren's Syndrome

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ABSTRACT. ***Objective.*** To identify the clinical characteristics, pathological changes, and outcome of patients with primary Sjögren's syndrome (pSS).

Methods. All patients with pSS and renal involvement who were admitted to Ruijin Hospital from April 1993 to December 2006 were included. All the data of clinical features and pathological changes were retrospectively analyzed. Forty-one patients underwent renal biopsies.

Results. Our study included 130 patients with pSS: 122 women and 8 men. Ages ranged from 16 to 68 years (mean 44.1 ± 11.52). Ninety-five patients (73.1%) developed renal tubular acidosis (RTA); 91 were found to have distal RTA. Nine patients presented with hypokalemic paralysis. Four patients developed Fanconi syndrome and 3 were proved to have nephrogenic diabetes insipidus. Twenty-seven of 130 patients (20.8%) developed tubular proteinuria and 18/130 (13.8%) presented glomerular involvement. Thirty-five patients (27.7%) developed renal failure (serum creatinine > 115 μmol/l). Most patients (70.8%) had increased serum IgG levels. The incidence of chronic interstitial nephritis was 80.5% among all the biopsy materials. Immunofluorescent staining was negative in most renal tissue. Ninety-six patients were treated with corticosteroids and/or immunosuppressant. Eighteen recovered renal function.

Conclusion. Patients with pSS commonly present with renal impairment, mainly from renal tubular dysfunction. The combination of corticosteroids and immunosuppressors significantly improves the renal function of patients with pSS. There is a correlation between hypergammaglobulinemia and distal RTA. The renal acidification capacity for patients with hypergammaglobulinemia should be monitored. (First Release Dec 15 2007; J Rheumatol 2008;35:278–84)

Key Indexing Terms:
SJÖGREN'S SYNDROME RENAL INVOLVEMENT CLINICAL PATHOLOGY

Sjögren's syndrome (SS) is an autoimmune connective tissue disorder that affects exocrine glands (especially lacrimal and salivary glands). It has a female predominance, with female to male ratio about 9:1, and its onset age is about 45–55 years. SS can be divided into primary SS (pSS) and secondary SS subgroups. pSS is defined as a kind of disorder not related to other systemic autoimmune diseases. The major clinical manifestation of pSS includes dryness of mouth and eyes. Other manifestations that affect skin, lungs, gastrointestinal tract, central and peripheral nervous systems, musculoskeletal apparatus, and kidney can also be found in certain patients[1-9]. A characteristic of SS is infiltration of plasmacytoid lymphocytes and circulating anti-SSA and anti-SSB antibody positivity. Renal involvement, among the most common manifestations of pSS, has no specific symptoms[10]. We retrospectively analyzed 130 cases of pSS with renal involvement in order to further study the disease.

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MATERIALS AND METHODS

Patient selection. One hundred thirty patients with pSS admitted to Shanghai Ruijin Hospital from April 1993 to December 2006 were enrolled. All the patients met the validated European-American co-criteria of 2002[11] for pSS. Renal involvement was present in all the patients. No patients with secondary SS were included.

Diagnostic criteria. (1) SS diagnostic criteria referred to the European-American co-criteria of 2002 (Table 1). With no evidence of potential disease, the diagnosis could be made when either patients fulfil 4 or more items in Table 1, and Item IV (histopathology) and/or Item VI (autoantibodies) should be included; or patients fulfil 3 items of Item III, IV, V, VI in Table 1.

(2) Significant renal involvement is defined by 1 or more of the following criteria: serum creatinine > 115 μmol/l or glomerular filtration rate (GFR) < 60 ml/min; persistent proteinuria (> 500 mg/24 h) for more than 3 months; urine red blood cells > 5 erythrocytes/high-power field on 2 separate occasions in the absence of urinary infection or red blood cell casts were present; persistently low specific gravity (< 1.010) associated with persistent urine pH

Table 1. European-American co-criteria.

I. Oral symptoms: at least one of
  1. Daily feeling of dry mouth for more than 3 mo
  2. Recurrent or persistently swollen salivary glands
  3. Use of liquids to aid in swallowing dry food
II. Ocular symptoms: at least one of
  1. Dry eyes every day for more than 3 mo
  2. Recurrent sensation of sand or gravel in the eyes
  3. Use of tear substitutes more than 3 times a day
III. Ocular signs: at least one of
  1. Positive Schirmer test (≤ 5 mm/5 min)
  2. Positive Rose Bengal score (≥ 4 van Bilsterveld scoring system)
IV. Histopathology:
  Patho-biopsy of infralabial gland shows lymphocyte focus ≥ 1 (one focus means there are at least 50 lymphocytes aggregated in glandulae matrix within 4 mm^2 tissue)
V. Salivary damage: at least one of
  1. Positive salivary flow testing (≥ 1.5 ml/15 min)
  2. Positive parotid sialography
  3. Positive salivary scintigraphy
VI. Autoantibodies: anti-SSA and/or anti-SSB antibody-positive (double diffusion method)

> 7 for more than 6 months; recurrent urolithiasis or nephrocalcinosis; or Fanconi syndrome.

Clinical observation items. Sex, age, duration from onset to diagnosis, duration of pSS and renal involvement, first starting symptom, glandular organ symptoms (dry mouth and eyes), extraglandular symptoms of SS (arthralgia, rash, Raynaud's sign, diuresis, nycturia, and gastrointestinal, respiratory, neurological, hematological and other systemic manifestations). A detailed interview of family history, work history, previous disease, previous and concurrent medications, drug hypersensitivity history, hypertensive disease, history of urinary tract infection, and urinary lithiasis was performed as well. Nephrotic syndrome was defined as urine protein > 3.5 g/24 h and serum albumin < 30 g/l. Glomerulonephritis (GN) was defined as urine protein 1.0–3.5 g/24 h with or without hematuria.

Laboratory examinations. (1) Routine assays: blood, urine, liver and renal function, estimated GFR (eGFR) calculated by Cockcroft-Gault and Modification of Diet in Renal Disease formula evaluation, erythrocyte sedimentation rate (ESR), plasma protein electrophoresis. (2) Immunology assays: immunoglobulin (IgG, IgA, IgM), rheumatoid factor (RF), antinuclear antibodies (ANA), anti-ssDNA, anti-dsDNA, anti-SSA, anti-SSB, anti-ribonucleoprotein (RNP) and anti-Smith antibodies, cryoglobulin, and cold agglutination test. (3) Renal tubular function assays: blood and urine potassium, sodium, chlorine, calcium, phosphorus analysis, 24 h urine protein excretion, urine protein electrophoresis, urine glucose for 24 h, uric acid, blood and urine α_1-microalbumin (α_1-MG), $ß_2$-microalbumin ($ß_2$-MG), blood pH, carbon dioxide combining power, urine microprotein, including retinol binding protein (RBP) and urine N-acetyl-ß-amino-glucosidase (NAG), blood and urine osmotic pressure tests. Urine titratable acid assay was performed to test urine pH, HCO_3^-, TA, and NH_4^+. Ammonium chloride loading test was applied to the patients with no typical manifestations or biochemical signs. Ammonium chloride (or calcium chloride for patients with liver diseases) 0.1 g/kg was administered orally for 3 days. On the third day, carbon dioxide combining power, blood pH, and urinary pH were tested. If blood pH and carbon dioxide combining power diminished while urine pH exceeded 5.5, it was defined as positive. (4) Other tests: lacrimal and salivary gland secretion test (Schirmer test), ^{99}Tc isotope scanning for parotid and submaxillary glands, minor labial biopsy, and eye examination.

Renal biopsy. Renal biopsy specimens were processed for both light microscopy and immunofluorescence. A classic direct technique using antibodies against IgA, IgG, IgM, C3, C4, C1q, fibrin, κ, and λ was performed.

Statistical analysis. Data were expressed as mean ± standard deviation. All statistical analysis was performed with SPSS 11.0 software. One-way analysis of variance was performed to analyze the means of different groups. A p value < 0.05 was considered statistically significant.

RESULTS

Clinical data. One hundred thirty patients were enrolled in our study, 122 women (93.9%) and 8 men (6.2%). The female:male ratio was 15:1. The mean age was 44.1 ± 11.52 years (range 16–88 yrs). Duration from onset to diagnosis ranged from 2 weeks to 20 years. One hundred four (80%) patients had xerostomia, 90 (69.2%) had dry eyes, and only 7 patients (5.4%) had hypertension. Mean systolic pressure was 118.71 ± 16.16 mm Hg and diastolic pressure 72.10 ± 12.50 mm Hg.

Renal involvement. Tubular disorders. Ninety-five of the 130 patients with pSS (73.1%) developed RTA; 91 of them had distal RTA (dRTA; 66 complete RTA, 25 incomplete RTA). Patients had polyposia, polydipsia, and impaired tubular proton secretion capacity. Typically, their urine pH was > 5.5 and urine potassium excretion was elevated. Some patients presented with hyperchloremia, hypokalemia, and metabolic acidosis. Incomplete RTA was identified by ammonium chloride loading test. Nine patients visited a nephrologist because of hypokalemic paralysis; one died from cardiac arrest. Four patients had Fanconi syndrome with tubular absorption disorders. Three patients had dRTA associated with nephrogenic diabetes insipidus, manifesting as low urine specific gravity, 4000 ~ 7000 ml of daily urine volume, persisting after water deprivation and vasopressin assay, with normal sella turcica by computerized tomography scan and radiography. Tubular proteinuria, defined as urine protein < 1 g/24 h and low molecular weight proteinuria by urine protein electrophoresis, was present in 20.8% of the patients (27/130). Concentration and dilution was abnormal, which included hydrouria, predominantly nycturia (> 750 ml). The difference between the maximal and minimal urine specific gravity was less than 0.008 (Table 2).

Table 2. Analysis of 130 pSS patients with renal tubular dysfunction (RTA).

	No.	%
RTA	95/130	73.1
Distal RTA (dRTA)	91/95	95.8
Complete dRTA	66/91	72.5
Incomplete dRTA	25/91	27.5
Fanconi syndrome	4/130	3.1
Nephrogenic diabetes insipidus	3/130	2.3
Tubular proteinuria	27/130	20.8
Increased urine $ß_2$-microalbumin	63/89	70.8
Increased NAG	19/70	27.1
Increased RBP	47/54	87.0
Urine concentration disorders	50/61	81.9

NAG: N-acetyl-ß-amino-glucosidase; RBP: retinol binding protein.

Glomerular impairment. Eight patients were diagnosed with nephrotic syndrome, 10 with GN. The incidence of glomerular impairment was 13.9% (18/130). Cryoglobulin and cold agglutination test were negative.

Renal function. Of 130 patients with renal involvement, the baseline blood urea nitrogen was 7.43 ± 11.20 mmol/l, and serum creatinine (Scr) was 116.78 ± 105.46 μmol/l. eGFR was 69.88 ± 31.97 ml/min. Of the 130 patients, 30 (26.9%) had Scr > 115 μmol/l.

Laboratory presentations. Blood, urine, and biochemical tests. Eight patients had leukocytopenia (6.2%); 9 patients had anemia (6.9%). The mean urine pH in the patients was 6.77 ± 1.12; the mean level of blood carbon dioxide combining power was 20.49 ± 4.95. The mean blood potassium level was 3.43 ± 0.86 mmol/l; 61 patients had hypokalemia (46.9%).

Immune abnormalities. Most patients presented with increased serum IgG (70.8%). The average serum IgG was 2224.11 ± 988.26 mg/dl. Increasing ESR was found in 89 patients (80.9%). Anti-SSA and/or anti-SSB antibody positivity was common, especially anti-SSA antibody (Table 3).

Renal pathology. Light microscopy. Thirty-three of 41 (80.5%) pSS patients with renal biopsy had chronic interstitial nephritis; plasmacytoid lymphocyte infiltration was present in most patients. Tubular atrophy was also observed. Three cases had proliferative GN with diffuse mesangial cellular hyperplasia and matrix thickening. One patient had membranous nephropathy. Mesangial proliferative nephritis was found in 2 cases. Two patients had focal segmental glomerulosclerosis (Figures 1 and 2).

Immunofluorescence. In the 41 patients with renal biopsy, 29 (70.7%) were negative by immunofluorescence. IgG deposits in the capillary walls were found in 2 patients. IgA deposits were found in 3 of 41 patients, where IgA was located in the mesangial regions. IgM deposits were found in 7 patients. Among those 7 patients, 4 patients had IgM segmentally deposited in mesangial regions, 2 had diffuse IgM deposits in mesangial regions, and 1 had diffuse IgM deposits in the capillary wall. C3 deposits were found in 6 patients and C4 deposits in one patient. One patient had IgG deposits in the interstitial cells.

Table 3. Immunologic function tests of patients with primary Sjögren's syndrome.

Index	No.	%
Increased IgG	92/130	70.8
ANA-positive	66/128	51.6
SSA-positive	66/130	50.8
SSB-positive	49/128	38.3
RNP-positive	9/115	7.8
RF-positive	59/101	58.4
Low C3	55/124	44.4
Low C4	18/124	14.5
Increased ESR	89/110	80.9

ANA: antinuclear antibodies; RF: rheumatoid factor; ESR: erythrocyte sedimentation rate.

Comparison of pSS patients with and without RTA. Except for the age and incidence of hypergammaglobulinemia, there were no statistical differences regarding hypertension, Scr, eGFR, level of proteinuria, urinary $ß_2$-MG, urinary NAG, urinary RBP, urine concentration and dilution function, ANA, anti-SSA antibody, anti-SSB antibody, and mean of serum IgG between the RTA and non-RTA groups of patients (Table 4).

Comparison of patients with interstitial nephritis and with GN. There were no statistical differences regarding age, duration of disease, incidence of dry eyes, Scr, ANA, anti-SSA antibody, anti-SSB antibody, or mean of serum IgG, RF, C4, ESR and cryoglobulins between the interstitial nephritis and GN patient groups, except for C3 depletion (Table 5).

Outcome. Thirty-four of 130 patients received symptomatic treatment. Sixty-four patients were treated with corticosteroids alone (0.5 mg/kg/day). Twelve patients received corticosteroids together with intravenous cyclophosphamide (CTX) therapy or oral CTX. Two took oral corticosteroids as well as *Tripterygium wilfordii*. The duration of followup ranged from 0.5 to 10 years. Except for 4 deaths (2 from infection, 1 from cerebrovascular accident, 1 from lymphoma), the remainder of the patients had good prognosis. Among the 35 patients with Scr > 115 μmol/l, 18 achieved normal renal function after therapy, 7 patients' renal function improved, 6 had no change, and the remaining 4 patients progressed to endstage renal dysfunction.

DISCUSSION

pSS is a type of autoimmune disease with multiple organs involved apart from exocrine glands. Renal involvement is one of the most common manifestations of pSS[10]. With improved testing facilities and methodologies, diagnosing pSS at an early stage has improved significantly. Due to different diagnostic criteria, the frequency of renal abnormalities varies from 18.4% to 67%[10,12-17]. The clinical manifestations of this disease are not identical. Some patients have no typical symptoms, while some are misdiagnosed[13]. However, few patients could die from manifestations of endstage renal failure. We concluded that the incidence of pSS was the second most common disease of all the autoimmune disorders with renal involvement in our department, after lupus nephritis.

Renal involvement of pSS is mainly manifested as tubular disorders, especially as dRTA. For physiological reasons, some patients might have paralysis resulting from hypokalemia[18], even respiratory muscle paralysis. Some patients have no clinical symptoms of RTA and their routine tests were normal, but ammonium chloride loading test was abnormal, which suggests the renal tubular dysfunction of secreting hydrogen and ammonium[19-21]. In our 130 patients, 95 (73.1%) presented with RTA and 91 had dRTA. There were more patients with complete RTA than with incomplete RTA. The high percentage of patients with RTA suggests that pSS is

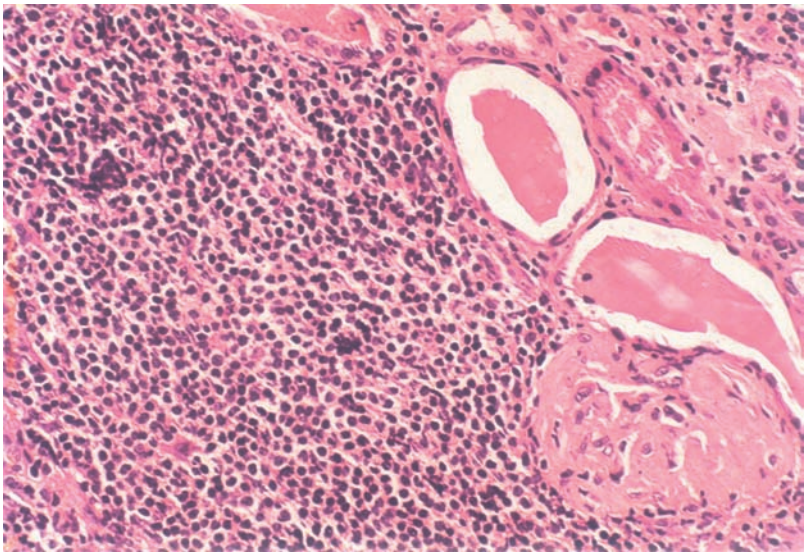

Figure 1. Diffuse interstitial lymphoplasmocellular infiltration (H&E ×400).

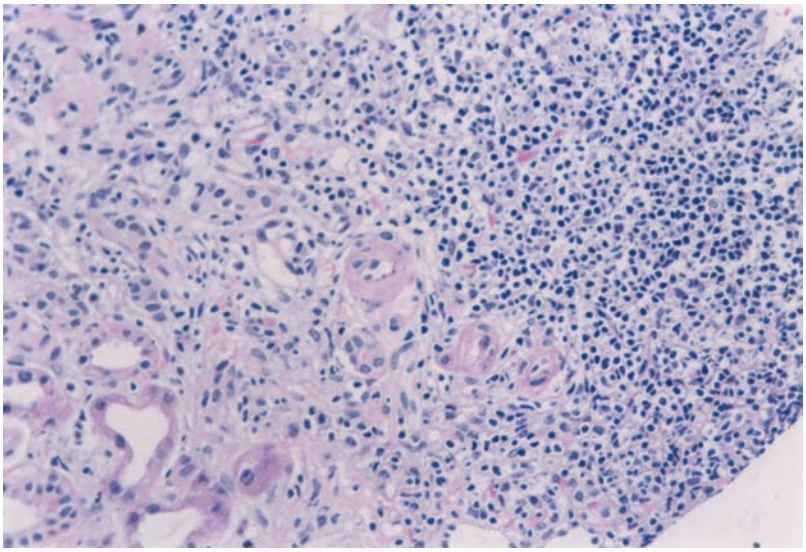

Figure 2. Diffuse interstitial lymphoplasmocellular infiltration and atrophic tubules (H&E ×400).

one of the most important causes of RTA. In our study, 61 (46.9%) patients had hypokalemia. Nine presented with hypokalemia paralysis, and 1 had asystole. All 61 patients had complete dRTA, suggesting hypokalemia is an important clue to diagnose RTA.

Proximal RTA is due to proximal renal tubular reabsorption of carbonic acid hydrogen ion functional disturbance. Urine loss of HCO^{3-} might be associated with reabsorption disorders of other various materials[22]. In our study, Fanconi syndrome was found in only 4 of the 95 patients with RTA, suggesting the incidence of proximate renal tubular injury in SS was much lower than that of distal renal tubular injury.

The incidence of RTA in patients with pSS was reported by various studies. In an early study by Talal, *et al*[23], incidence of RTA in 10 pSS and 2 sSS patients was 50%. In a retrospective study of 171 patients with pSS, tubular acidification ability disturbance was found in 25%[24]. In other studies, incidence of RTA was between 33% and 48%[17,25-27]. In a study by Eriksson, *et al*, incidence of dRTA was 67% among 27 female patients with pSS[28]. In our study, the incidence of RTA was 73.1%, which was higher than in previous reports. It was probably due to RTA being the main and first symptom of our patients.

In our study, lower urine concentration was found in 50 (81.9%) of 61 patients with pSS. Hyperuresis was mainly found as nycturia (> 750 ml). There were 3 dRTA patients with renal diabetes insipidus. Since systematic investigations on urinary concentration of patients with pSS are rare and the assay methods have not been unified, the reported incidence

Table 4. Comparison of some clinical and laboratory findings in pSS patients with and without RTA.

Variable	With RTA, n = 95	Without RTA, n = 35	p
Age, mean, yrs	42.45 ± 11.74	46.35 ± 10.77	< 0.05
Duration of the disease, yrs	3.48 ± 4.21	3.71 ± 4.93	NS
Frequency of hypertension, % (n)	6.56 (4/61)	12 (3/25)	NS
Serum creatinine, μmol/l	116.94 ± 90.78	123.34 ± 148.19	NS
GFR, ml/min (MDRD formula)	67.49 ± 31.52	74.28 ± 33.29	NS
Frequency of proteinuria (> 150 mg/24 h), % (n)	73.5 (61/83)	75 (21/28)	NS
Increased urine ß$_2$-microalbumin, % (n)	77.4 (41/53)	88 (22/25)	NS
Increased urine NAG, % (n)	27.5 (14/51)	26.3 (5/19)	NS
Increased urine RBP, % (n)	89.7 (35/39)	80 (12/15)	NS
Urine concentration problem, % (n)	86.7 (39/45)	68.8 (11/16)	NS
ANA-positive, % (n)	53.7 (51/95)	45.7 (16/35)	NS
Anti-SSA-positive, % (n)	49.5 (47/95)	54.3 (19/35)	NS
Anti-SSB-positive, % (n)	36.8 (35/95)	41.2 (14/34)	NS
Serum IgG, g/l	2305.57 ± 983.28	1974.71 ± 967.2	NS
Frequency of hypergammaglobulinemia, % (n)	80 (76/95)	54.3 (19/35)	< 0.01

pSS: primary Sjögren's syndrome; RTA: renal tubular acidosis; GFR: glomerular filtration rate; NAG: N-acetyl-ß-amino-glucosidase; RBP: retinol binding protein; ANA: antinuclear antibodies. NS: not significant.

Table 5. Comparison of interstitial nephritis (IN) and glomerulonephritis (GN) groups.

Variable	IN, n = 99	GN, n = 18	p
Age, mean, yrs	43.41 ± 11.74	44.11 ± 12.22	NS
Duration of the disease, yrs	2.69 ± 4.99	3.94 ± 4.54	NS
Dry mouth, % (n)	87.5 (77/88)	93.3 (14/15)	NS
Dry eyes, % (n)	72.7 (64/88)	86.7 (13/15)	NS
Serum creatinine, μmol/l	114.18 ± 90.52	145.86 ± 183.43	NS
Anti-SSA-positive, % (n)	52.1 (49/94)	38.9 (7/18)	NS
Anti-SSB-positive, % (n)	39.8 (37/93)	27.8 (5/18)	NS
Serum IgG, g/l	2187.02 ± 927.29	2410.28 ± 1414.48	NS
RF, % (n)	54.3 (38/70)	64.7 (11/17)	NS
Low C3, % (n)	45.6 (49/90)	17.6 (3/17)	< 0.05
Low C4, % (n)	13.2 (12/91)	11.8 (2/17)	NS
Increased ESR, % (n)	71.3 (67/94)	64.7 (11/17)	NS
Cryoglobulins	0	0	

ESR: erythrocyte sedimentation rate; NS: not significant.

ranged from 16% to 82%. Therefore, it is not a rare clinical manifestation but might be an indicator of renal injury in early stages[10,13,16,29]. Our study had similar results.

We found tubular proteinuria in 27 of 130 patients with urine protein < 1 g/24 h. Urine protein electrophoresis showed low molecular weight proteinuria. In a study by Aasarød, *et al*[10], mild proteinuria was found in 44% of patients with pSS and their blood pressure, ß$_2$-MG level, and incidence of impairment of urine acidification were all higher than in those without proteinuria. In a previous study, ß$_2$-MG, NAG, and RBP as a marker protein reflecting impaired proximal tubular function in patients with pSS, were elevated at different levels. In addition, the serum levels in the RTA group were apparently higher than in the non-RTA group[10,29]. In our study, increased level of ß$_2$-MG, NAG, and RBP were observed in 70.8%, 27.1%, and 87.0% of patients, respectively. Incidence of elevated ß$_2$-MG and RBP (but not NAG) was higher in our patients, compared with previous reports. There were no differences in RTA and non-RTA groups.

Glomerular lesion is not common in pSS and the manifestations might be hematuria, proteinuria, or even nephrotic syndrome. In a study by Bossini, *et al*[13], the incidence of glomerular lesion was 5%. In our study, glomerular proteinuria was found in 18 (13.9%) of 130 patients. However, glomerular lesion is not the main type of renal involvement in SS. If glomerular lesion is found, it might be associated with systemic lupus erythematosus or combined cryoglobulinemia. The pathogenesis of glomerular lesion remains unclear; circulating immune complex deposits might be an important factor. One study proposed that the presence of purpura, low C4 complement, and mixed monoclonal type II cryoglobulinemia might predict glomerular lesion[30].

There have been several different reports regarding renal dysfunction in SS. Impaired GFR was found in 21% of patients with pSS by Aasarød, *et al*[10]. A retrospective study by Vitali, *et al*[12] found only 2% of patients with pSS presented with GFR < 60 ml/min. However, another study found the incidence of decreased GFR was 33%[31], which might be related to higher incidence of RTA and renal calculus. In our study, Scr > 115 μmol/l was found in 35 (26.9%) of 130 patients with renal involvement (Scr was 116.78 ± 105.46 μmol/l at disease onset). GFR < 60 ml/min was found in 39% of them. The incidence of renal failure is higher than in previous studies. This is probably due to a higher proportion of renal tubular injury in our study.

The incidence of hypergammaglobulinemia in our patients with pSS was 70.8%, while in other reports it was almost 50%. The possible role of hypergammaglobulinemia in the occurrence of RTA has been suggested by several studies[23,32-34]. By contrast, Pasternack, *et al*[35] proposed that hypergammaglobulinemia was not involved in the abnormal acidification present in rheumatoid arthritis. This result was confirmed by subsequent research[12,16,17,25]. Aasarød, *et al*[10] found that serum IgG in the dRTA group was higher than that in the non-dRTA group, but there was no statistical difference. Pertovaara, *et al*[29] had similar results; however, they proposed that the frequent use of corticosteroids in the dRTA group might affect concentration of circulating IgG. We observed that the incidence of hypergammaglobulinemia was 80% in the dRTA group and 54.3% in the non-dRTA group ($p < 0.01$), which suggested a possible relationship between hypergammaglobulinemia and dRTA. Further, it was observed in other studies that ANA, anti-SSA antibody, and anti-SSB antibody might be associated with RTA, since there was a higher proportion of patients with those antibodies in the RTA group than in the non-RTA group[10,29].

The characteristic histological feature of pSS is chronic interstitial nephritis, with diffuse or focal plasmacytoid lymphocytic infiltration. In the late stage of disease, tubulointerstitial fibrosis is severe[36,37]. Immunofluorescence shows few immune deposits. Plasmacytoid lymphocytic infiltration is regarded to be an important predictive factor for the activity of the disease. Our study identified 33 cases of chronic interstitial nephritis, which was slightly higher than reported in other series[13]. It had been suggested that few patients with pSS had GN. Bossini, *et al*[13] reported 3 cases of GN in 9 patients with pSS, which included membranous nephropathy, membranoproliferative GN, or mesangial proliferative nephritis. In our study, of all the 41 renal biopsy cases, 3 were mesangial proliferative GN, 1 membranous nephropathy, 2 membranoproliferative GN, and 2 FSGS, which suggested that the glomerular lesions were still present. The mechanism of glomerular lesions may be related to immune complex deposition, cryoglobulinemia, and low C4.

By comparing the age, course of pSS and renal impairment, clinical manifestations, and immune abnormalities between the interstitial nephritis group and the GN group, Goules, *et al*[38] proposed that (1) in the interstitial nephritis group, the patients were younger, and the courses of renal impairment were shorter; (2) in the GN group, the incidence of cryoglobulinemia and low C4 was higher; (3) interstitial nephritis usually occurred in the early stage, while GN developed in the late stage of the disease and the prognosis of the patients with GN was poor. In our study, incidence of low C3 was statistically different between the 2 groups, but there were no differences regarding age, disease course, clinical manifestations, renal function, and immunological abnormality. Cryoglobulinemia was not found in either group.

In our study, of the 130 patients with pSS, 96 were treated with corticosteroids with or without immunosuppressant, while the remaining 34 were not treated with corticosteroids or immunosuppressants. The duration of followup ranged from 0.5 to 10 years. Except for 4 deaths, the others had good prognosis. Eighteen of the 35 patients with Scr exceeding 115 μmol/l had recovered renal function after treatment, and 7 had improved renal function. Few studies have evaluated the efficacy of corticosteroids and immunosuppressant in pSS. Saeki, *et al*[39] reported 1 case of pSS with renal impairment whose clinical manifestations and serum and histological findings significantly improved after high-dose and maintenance dose of corticosteroids. Also, the study of Miyawaki, *et al*[40] revealed that the serum level of IgG, anti-SSA antibody, anti-SSB antibody, and RF decreased in 20 cases of pSS after therapy with corticosteroids. Thus, it is likely that corticosteroids and/or immunosuppressive therapy may improve the prognosis for certain patients with pSS, especially those with interstitial pneumonia, neuropathy, renal involvement, or hypergammaglobulinemia.

In summary, we found that pSS with renal impairment was common; renal tubular disorders, especially dRTA, was predominant; pSS may be correlated with hypergammaglobulinemia; the impairment of urinary concentration was a common and initial sign; sometimes, glomerular lesions might be predominant and correlated with the decreased level of C4; morbidity of chronic renal failure might account for a certain proportion of pSS; chronic interstitial nephritis was a typical pathological feature of pSS, and the pathological progression correlated with the impairment of renal function; and that corticosteroids or/and immunosuppressant therapy might improve the prognosis.

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