Clinical And Morphological Features Of Kidney Involvement In Primary Sjögren's Syndrome

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Introduction

Sjögren's syndrome is an autoimmune disorder belonging to the group of the chronic systemic rheumatic diseases. The principal target organs are the exocrine glands. However, several non-exocrine organ systems may also be involved, including skin, lung, gastrointestinal tract, central and peripheral nervous system, muscular skeletal apparatus, and the kidney. In the affected organs, the key histological feature is a focal or diffused lymphoid infiltration, predominantly represented by CD4 T lymphocytes (1).

The presence of renal involvement in Sjogren's syndrome has been known since the 1960s. Most commonly, a tubulointerstitial nephritis with defects in tubular function has been found (4,7). However, glomerular diseases such as membrano-proliferative glomerulonephritis and membranous nephropathy, have also been reported (2, 6).

In this report, we evaluated the prevalence of kidney involvement in 46 Bulgarian patients with primary Sjogren's syndrome and analysed whether this disorder is a cause of renal impairment. Our purpose was to examine relationships between the clinical and serological features of the syndrome and the presence of renal disease.

Patients and methods

We studied the nature of kidney involvement in 46 patients with primary Sjogren's syndrome, diagnosed according to the European classification criteria (ocular symptoms, oral symptoms, evidence of keratoconjuctivitis sicca, focal sialoadenitis by minor salivary gland biopsy, instrumental evidence of salivary gland involvement, and presence of autoantibodies Ro/SSA and or La/SSB. No patients fulfilled the diagnostic criteria for other connective tissue disease or autoimmune disorders. A detailed anamnestic investigation was carried out to detect urinary tract infection, urolithiasis, and intake of non-steroidal anti-inflammatory drugs, in order to exclude possible causes of tubular dysfunction. The existence of hypertension was defined as previous or current use of antihypertensive drugs.

The patients underwent the routine laboratory tests and renal laboratory investigations. A percutaneous renal biopsy was proposed to patients, presenting with a variable reduction of creatinine clearance, tubular defects, and urinary abnormalities. Signs of renal involvement, such as urine abnormalities and tubular defects, were most commonly identified in the absence of apparent clinical manifestations.

Results

Table 1 summarizes epidemiological data and clinical extraglandular manifestations observed in the 46 patients. Extraglandular involvement was frequently present. The serological findings and the results of routine nephrological tests and tubular function tests are shown in Table 2.

Two patients had overt nephrotic syndrome and three patients had a history of recurrent stone disease complicated by nephrocalcinosis. A variable reduction in creatinine clearance (usually slight – range 45-70 ml/min) was found in 6 patients (13,04 %). Proteinuria was found in 11 patients (23,91 %): in 9 patients - protein excretion was less than 1g/24 h, in 1 patient - 1,5-2 g/24 h and in 2 patients – in the nephrotic range. Microscopic haematuria was associated with proteinuria in five patients. None of the patients showed renal glucosuria and/or hypophosphatemia.

Nine patients with kidney involvement agreed to undergo renal biopsy. In 6 patients mild to severe tubulo-interstitial nephritis was found - it was characterized by focal or diffuse lymphoplasmo- cellular infiltrate of mononuclear cells with variable tubular atrophy and mild to intense interstitial fibrosis. Chronic glomerulonephritis was diagnosed in three patients (membranous nephropathy – in 1 and membranoproliferative – in 2 patients).

Discussion

Since there is as yet no single specific symptom or test to accurately diagnose Sjogren's syndrome, various criteria sets have been proposed by different authors (3,5). Our study was designed to evaluate the frequency of renal involvement in a large group of patients with primary Sjogren's syndrome diagnosed according to the European classification criteria (9). The prevalence and type of renal involvement in primary Sjogren's syndrome are unclear. In the literature, the frequency of renal abnormalities varies from 16 to 67% (4,7,8). Several reasons may account for this discrepancy. The first is that only small groups of patients with Sjogren's syndrome were studied for renal involvement. The second is the lack of well-defined and commonly accepted criteria for diagnosing primary Sjogren's syndrome. Third, in some studies, primary and secondary forms of Sjogren's syndrome were analysed together making it difficult to understand whether renal involvement should be ascribed to Sjogren's syndrome per se, or to associated disorders. Thus, the true prevalence of renal disease in primary Sjogren's syndrome remains uncertain,

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and studies involving larger patient groups with diagnoses according to highly valid and reliable criteria are still needed.

Our study suggests that clinically evident renal disease is rare in patients with primary Sjogren's syndrome and that the presence of subclinical renal dysfunction, usually ascribed to tubulo-interstitial nephritis of variable degrees, may be detected by means of appropriate tests. The patients with Sjogren's syndrome showing tubular defects were significantly younger and had a shorter disease duration. A lower creatinine clearance and ANA was more frequent in patients with abnormal tubular tests, suggesting that more severe autoimmunity may increase the risk of renal involvement.

Table 1. Epidemiological and clinical features of 48 patients with primary Sjogren's syndrome.

NUMBER OF PATIENTS	46	
SEX	44 F/2 M	
AGE (YEARS)	48 (22-64)	
MEAN DURATION OF DISEASE (YEARS)	5 (0-14)	
ARTHRALGIA/ARTHRITIS	36	75%
MYALGIA	5	10,41%
RAYNAUD'S PHENOMENON	18	37,5%
PURPURA/VASCULITIS SKIN	11	22,92%
PERIPHERAL/CRANIAL NEUROPATHY	13	27,08%
INTERSTITIAL LUNG DISEASE	1	2,08%
THYREOIDITIS	2	4,16%
AUTOIMMUNE CHOLANGITIS	1	2,08%
RECURRENT URINARY INFECTION	1	2,08%
NEPHROLITHIASIS	1	2,08%
ARTERIAL HYPERTENSION	15	31,25%

Table 2. Serological findings and results from routine nephrological and tubular function tests in 48 patients with primary Sjogren's syndrome

	NUMBER OF PATIENTS	%
ANA	40	83,33%
ANTI-RO ANTIBODY	38	79,16%
ANTI-LA ANTIBODY	19	39,58%
RHEUMATOID FACTOR	39	81,25%
CRYOGLOBULINAEMIA	6	12,5%
LOW C3	4	8,33%
LOW C4	9	18,75%
HYPERGAMMAGLOBULINAEMIA	35	72,91%
HIGH ESR	31	64,58%
HIGH CRP	8	16,66%
ANAEMIA	3	6,25%
HCV ANTIBODY	4	8,33%
RENAL FAILURE	6	12,5%
METABOLIC ACIDOSIS	2	4,17%
HYPOKALIEMIA	3	6,25%
MORNING URINE pH > 5,5	15	31,25%
PROTEINURIA < 1 g/24 h	8	16,67%
PROTEINURIA 1,5-2 g/24 h	1	2,43%
NEPHROTIC PROTEINURIA	2	4,17%
MICROSCOPIC HAEMATURIA	4	8,33%
GLUCOSURIA	0	0%

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