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Renal Vein Thrombosis Suggestive of Extramembranous Glomerulonephritis Associated with Sjögren's Syndrome (Case Report)

Mariam El Galiou[1], Mina Agrou[1], Rihab Dkhissi[1], Loubna Benamar[1], Naima Ouzeddoun[1], Lamyae Rouass[2], Tarik Bouattar[1]

[1]Department of Nephrology Dialysis and Transplantation, IbnSina University Hospital, Mohamed V University, Rabat, Morocco
[2]Department of Pathological Anatomy, IbnSina University Hospital, Mohammed V University, Rabat, Morocco
Email: mariam6.9595@gmail.com

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Abstract

Introduction: Glomerular damage during Gougerot-Sjögren syndrome is much rarer than interstitial damage, and is essentially extra-membranous and membrano-proliferative glomerulonephritis. **Observation:** We report the case of a 44-year-old woman with primary Sjögren's syndrome, confirmed by clinical dryness syndrome, positive anti-SSA and anti-SSB antibodies, and a salivary gland biopsy revealing grade 4 lymphocytic sialadenitis according to CHISHOLM's classification. Later, the patient developed nephrotic syndrome, along with hypertension. Renal function remained normal with a creatinine level of 9.3 mg/l, and hematuria was absent. Only antinuclear antibodies tested positive, while anti-PLA2R antibodies were negative. A renal biopsy was performed, which was complicated on the same day by hemodynamic instability with hematuria. Renal CT scan with contrast injection revealed a posterior perirenal hematoma without contrast extravasation. Additionally, bilateral renal vein thrombosis was incidentally discovered, suggesting extramembranous glomerulonephritis. The patient's hemodynamic status stabilized after fluid resuscitation with isotonic saline solution (0.9%), without the need for blood transfusion. Renal biopsy confirmed extramembranous glomerulonephritis with interstitial fibrosis and minimal tubular atrophy. The initial etiological assessment was negative. The patient was started on oral corticosteroids, angiotensin-converting enzyme inhibitors, and therapeutic anticoagulation for renal vein thrombosis. The patient's condition improved, with the disappearance of the syndrome and spontaneous regression of the hematoma. **Discussion:** The association of nephrotic syndrome and renal vein thrombosis primarily suggests glomerulopathy, in particular ex-

tra-membranous glomerulonephritis. Sjögren's syndrome can be associated with extra-membranous glomerulonephritis without being its direct cause. Like, it is possible that it is a cause of glomerulonephritis, essentially extra membranous and membrano-proliferative. **Conclusion:** Sjögren's syndrome is generally underestimated cause of glomerulonephritis, which should be considered in cases of extra-membranous glomerulonephritis.

Keywords

Sjögren's Syndrome, Extramembranous Glomerulonephritis, Nephrotic Syndrome, Anti-PLA2R Antibodies

1. Introduction

Sjögren's syndrome (SS) is a systemic autoimmune disease characterized by lymphocytic infiltration of exocrine glands, mainly the salivary and lacrimal glands, and the production of autoantibodies [1].

Renal involvement in primary Sjögren's syndrome is primarily related to lymphoplasmacytic infiltration of the interstitium, leading to fibrosis. This condition can result in urinary concentration disorders, tubular acidosis, Fanconi syndrome, nephrogenic diabetes insipidus, nephrocalcinosis, and/or renal lithiasis [2]. Glomerular involvement in Sjögren's syndrome is much rarer and is dominated by two histological types: membranoproliferative and extramembranous glomerulonephritis [3].

We are treating the case of a woman followed for gougerot's disease and in whom renal vein thrombosis revealed extra-membranous glomerulonephritis.

2. Observation

We report the case of a 44-year-old woman followed for 3 years for primary Sjögren's syndrome, confirmed by clinical dryness syndrome, positive anti-SSA and anti-SSB antibodies, and a salivary gland biopsy revealing grade 4 lymphocytic sialadenitis according to CHISHOLM's classification.

The patient later developed nephrotic syndrome, for which she was admitted to the nephrology department. Clinical examination at admission revealed a conscious patient with a Glasgow Coma Scale (GCS) of 15/15, in good general condition, hypertensive at 150/91 mmHg, with a heart rate of 79 bpm, and eupneic with oxygen saturation of 98% on room air. Laboratory investigations showed hypoproteinemia at 43 g/l, hypoalbuminemia at 15 g/l, and proteinuria at 9 g/24 hours. Renal function remained normal with a creatinine level of 9.3 mg/l, and hematuria was absent (**Table 1** and **Table 2**). Antinuclear antibodies, anti-SSA antibodies, and anti-SSB antibodies tested positive. Anti-PLA2R antibodies and anti-DNA antibodies were negative. Antiphospholipid antibodies were negative. Complement fractions C3 and C4 were not consumed (**Table 3**). Serologies for viral hepatitis B, C, and HIV were negative.

A renal biopsy was performed, which was complicated on the same day by hemodynamic instability with hematuria. Renal CT scan with contrast injection revealed a posterior perirenal hematoma measuring 56.8 × 24.2 mm without contrast extravasation. Additionally, bilateral renal vein thrombosis was incidentally discovered, initially suggesting extramembranous glomerulonephritis. After fluid resuscitation with isotonic saline solution (0.9%), without the need for blood transfusion, the patient's hemodynamic status stabilized. Hemoglobin levels decreased from 13 g/dl to 12.2 g/dl and remained stable at a level above 12.5 g/dl (Table 4). The renal biopsy confirmed extramembranous glomerulonephritis with interstitial fibrosis and minimal tubular atrophy (Figure 1 and Figure 2). The initial etiological assessment was negative. The patient started oral corticosteroid therapy at a dose of 1 mg/kg/day for 6 months, followed by a gradual taper, in addition to an angiotensin-converting enzyme inhibitor and therapeutic anticoagulation with vitamin K antagonist for renal vein thrombosis. The patient's condition improved, with disappearance of the nephrotic syndrome, proteinuria controlled at 0.082 g/day after one year, and a creatinine level of 8.8 mg/l, as well as spontaneous regression of the hematoma.

Table 1. Laboratory results (chemistry) on admission, at 6 months, and 3-years follow-up.

	Admission	6 months	3 years
Blood urea (g/l) (0.15 - 0.55)	0.46	0.41	0.51
Creatinine (mg/l) (5.7 - 12.5)	9.3	8.2	8.7
eGFR (ml/min/1.73m²)	65	76	70
Uric acid (mg/L) (26 - 60)	57	52	49
Na+ (mEq/L) (136 - 146)	137	138	135
K+ (mEq/L) (3.5 - 5.1)	4.2	4.5	3.9
Calcium (mg/L) (84 - 102)	85	87	83
Phosphate (mg/L) (23 - 47)	31	28	25
Plasma glucose (g/L) (0.7 - 1.1)	0.9	1.0	0.94
Total protein (g/l) (64 - 83)	43	60	69
Albumin (g/l)	15	32	35
AST (U/L) (5 - 35)	19	23	26
ALT (U/L) (0 - 55)	24	35	29
Ferritine (ng/ml) (4 - 204)	150	158	123
TSH us (µUI/mL) (0.35 - 4.94)	0.98		
FT3 (pg/mL) (1.71 - 3.71)	2.54		
FT4 (ng/dL) (0.7 - 1.48)	1.23		

eGFR: Estimated glomerular filtration rate, **AST:** Aspartate transaminase, **ALT:** Alanine transaminase, **TSH:** Thyroid-stimulating hormone, **AST:** Aspartate transaminase, **ALT:** Alanine transaminase, **TSH:** Thyroid-stimulating hormone.

Table 2. Laboratory results (urinalysis) on admission, at 6 months, and 3-years follow-up.

	Admission	6 months	3 years
Urine red blood cells(/mm³) (<15)	6	2	4
Urine white cells (/mm³) (<10)	1	1	2
Proteinuria (g/day) (<0.3)	9	0.6	0.23

Table 3. Laboratory results (immunological tests) on admission.

	Admission
C3 (g/l) (0.83 - 1.93)	1.23
C4 (g/l) (0.15 - 0.57)	0.35
ANA	Positive
Anti-ds DNA antibodies	Negative
ANCA	Negative
AntiSMantibodies	Négative
AntiSSAantibodies	Positive
AntiSSBantibodies	Positive
APL antibodies	Negative
AntiPLA2R antibodies	Negative

ANA: Antinuclear antibodies, **Anti dsDNA:** Anti-double-stranded DNA antibody, **ANCA:** Antineutrophil cytoplasmic antibodies, **Anti-SM:** Anti-Smith antibody, **APL:** Antiphospholipid, **PLA2R:** Anti-phospholipase A2 receptor antibodies.

Table 4. Laboratory results (complete blood count) on admission, at 6 months, and after 3 years follow-up.

	Admission	6 months	3 years
White blood cell (µL) (4000 - 10,000)	6900		
Neutrophil (%)	67.4		
Lymphocyte (%)	20.2		
Eosinophil (%)	1.8		
Basophil (%)	0.4		
Monocyte (%)	10.2		
Hemoglobin (g/dL) (11.5 - 15.5)	13	12.7	13.2
Platelet (/µL) (150,000 - 400,000)	174,000		

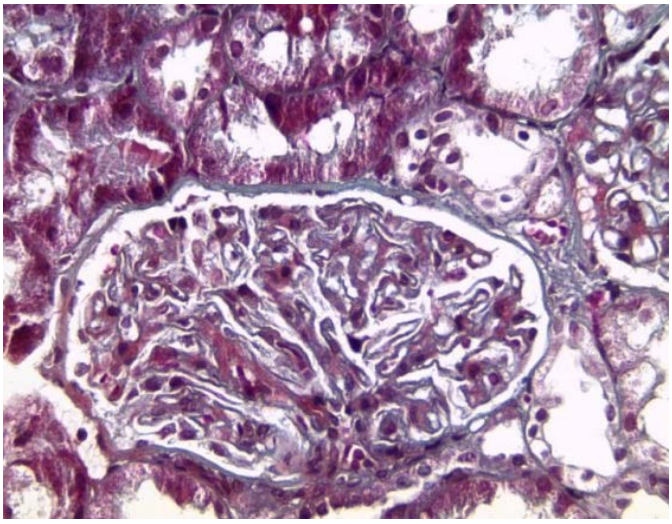

Figure 1. A glomerulus at high magnification: diffuse thickening of capillary walls and rigid lumens. Green trichrome, × 40.

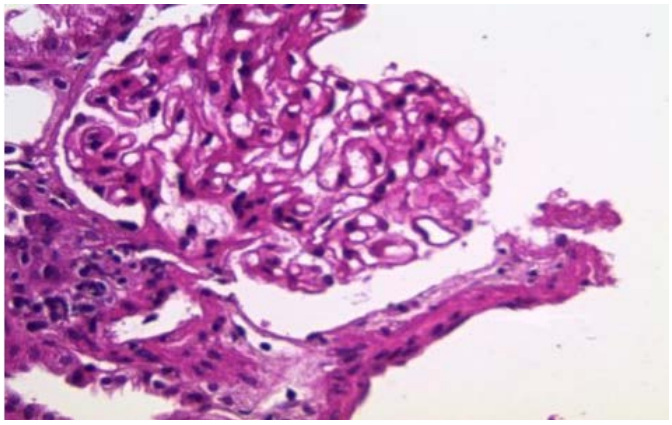

Figure 2. Glomerulus with its vascular pole. Overall thickening of capillary walls. Absence of endo-or extracapillary hypercellularity.

3. Discussion

The kidney is a potential target organ in Sjögren's syndrome. Most often, renal involvement is discovered years after the identification of the syndrome. Conversely, renal involvement can be the inaugural manifestation in a small number of patients: systematic investigation of extrarenal signs may lead to the diagnosis of Sjögren's syndrome.

The two varieties of lesions observed in "Sjögren's kidney" represent counterparts of the two major immunopathological abnormalities of the systemic condition: inflammatory infiltrate in exocrine glands and circulating immune complex disease. These two processes give rise, respectively, to chronic interstitial nephropathy or immune complex glomerulonephritis.

Glomerulonephritis in primary Sjögren's syndrome is considered rare, and this association may be underestimated since this connective tissue disorder is often only considered in the presence of dry syndrome. Therefore, this diagnosis

should be considered in the presence of various manifestations such as polyarthritis or hypergammaglobulinemia, but also in the presence of glomerulonephritis, as suggested by several observations reported in the literature [4] where the diagnosis was made on the biopsy of accessory salivary glands, systematically coupled with renal biopsy.

The association of nephrotic syndrome and renal vein thrombosis initially suggests a glomerulopathy, particularly extramembranous glomerulonephritis [5]. Primary Sjögren's syndrome may be associated with extramembranous glomerulonephritis without being its direct cause. It is possible that SS could be a cause of glomerulonephritis, primarily extramembranous and membranoproliferative. Despite renal vein thrombosis, the patient's renal function remained normal, and complete remission was achieved under corticosteroid therapy.

In our patient with primary Sjögren's syndrome, upon discovery of bilateral renal vein thrombosis, extramembranous glomerulonephritis was suspected and confirmed by renal biopsy. (**Figure 1** and **Figure 2**)

Tubulointerstitial involvement, which may or may not be symptomatic clinically or biologically, is histologically found in approximately 25% of patients with primary Sjögren's syndrome [2]. Glomerular nephropathies are much rarer, with fewer than 40 cases reported in the literature [6], with a prevalence estimated at 2% in a cohort of 471 Greek patients [7].

Glomerulonephritis with deposits are the most common (about thirty cases) and are evenly distributed between membranoproliferative forms [8] and extramembranous forms [9], and sometimes associated. Subsequently, pauci-immune glomerulonephritis (without deposits in immunofluorescence) has been reported, including crescentic (extracapillary proliferative) forms, associated [9] [10] or not with anti-neutrophil cytoplasmic antibodies (ANCA) of the p-ANCA (anti-MPO) type.

The evolution of glomerulonephritis in primary SS varies according to the histological type. Generally, if SS-associated glomerulonephritis has a favorable prognosis under medium-dose corticosteroid therapy (approximately 0.5 mg/kg/day of prednisone) [11], they can nevertheless rarely lead to chronic kidney failure [7] [11], highlighting the need for vigilant management.

In our patient, the discovery of extramembranous glomerulonephritis on renal biopsy prompted us to initiate full-dose corticosteroid therapy for 6 months, followed by a gradual tapering of corticosteroid dosage. The patient's condition improved, marked by the disappearance of nephrotic syndrome, with a proteinuria level <0.1 g/day after 3 years, and a creatinine level of 8.8 mg/l. Additionally, therapeutic anticoagulation with vitamin K antagonist was initiated for bilateral renal vein thrombosis secondary to extramembranous glomerulonephritis.

4. Conclusion

Sjögren's syndrome is a generally underestimated cause of glomerulonephritis, which should be considered in cases of extramembranous glomerulonephritis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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