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Case Report

Lupus nephritis with massive subendothelial deposits in a patient with autoimmune hepatitis-related cirrhosis

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ABSTRACT

A 72-year-old Japanese woman with a history of autoimmune hepatitis-associated liver cirrhosis and portosystemic shunt was admitted to our hospital for evaluation of renal dysfunction, nephrotic range proteinuria, a high titer of anti-double-stranded DNA antibody, and hypocomplementemia. Renal biopsy showed massive subendothelial deposits (wire loop lesions), and class IV-G (A/C) lupus nephritis was diagnosed. Immunosuppressants, such as steroids (including intravenous methylprednisolone pulse therapy) and mycophenolate mofetil, could not prevent renal dysfunction. It was assumed that circulating immune deposits produced in the gastrointestinal tract entered the systemic circulation from the portal vein via the portosystemic shunt without hepatic clearance, resulting in massive subendothelial and mesangial accumulation compared to lupus nephritis patients without a shunt and causing renal injury.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that affects the kidneys in about 50% of patients, with renal involvement being called lupus nephritis (LN). In SLE patients, LN is a major determinant of morbidity and mortality, and it progresses to end-stage renal disease (ESRD) despite potent immunosuppressive therapy [1]. Various factors contribute to development of chronic kidney disease/ESRD following acute or subacute renal injury in SLE patients, including inflammation, activation of intrinsic renal cells, cellular stress and hypoxia, metabolic abnormalities, aberrant tissue repair, and tissue fibrosis [2]. In patients with LN, deposits of immune complexes are well known to be more abundant compared to patients with other types of proliferative glomerulonephritis such as IgA nephropathy. Although “wire loop” lesions due to deposition of immune complexes are suggestive of LN, the meaning of these structures remains unknown.

We encountered a patient with LN and massive subendothelial deposits that were far more extensive than in other patients with LN. The possible pathogenesis of these massive deposits is discussed in relation to this patient's portosystemic shunt and liver cirrhosis.

2. Case report

A 72-year-old Japanese woman was referred to our hospital for evaluation of rapidly progressive renal dysfunction and nephrotic range proteinuria. Liver dysfunction was first detected at the age of 60 years. A definite diagnosis of autoimmune hepatitis (AIH) was made according to the revised scoring system of the International Autoimmune Hepatitis Group [score of 16: female (+2), AST ratio (+2), IgG level (+1), antinuclear antibody (+3), viral markers (+3), drug (+1), alcohol (+2) and autoimmune disease (+2)] [3]. Ultrasonography and contrast-enhanced computed tomography (CT) demonstrated liver cirrhosis with a portosystemic shunt including dilatation of paraumbilical veins. Esophageal varices were treated by endoscopic variceal ligation.

Abbreviations: IC, immune complexes; EDD, electron-dense deposits; SLE, systemic lupus erythematosus; LN, lupus nephritis; ESRD, end-stage renal disease; MPGN, membranoproliferative glomerulonephritis; eGFR, estimated glomerular filtration rate; LM, light microscopy; IF, immunofluorescence; anti-ds-DNA, anti-double-stranded DNA; ITIM, immunoreceptor tyrosine based inhibitory motif; ISN/RPS, International Society of Nephrology/Renal Pathology Society; RPGN, rapidly progressive glomerulonephritis

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Table 1
Laboratory data on admission.

	Onset	Normal range		Onset	Normal range
White blood cell (/μL)	3800	3200–7900	IgG (mg/dL)	1314	870–1700
Red blood cell ($\times 10^6$/μL)	2.99	3.7–5.7	IgA (mg/dL)	361	110–410
Hemoglobin (g/dL)	9.6	11.3–15.0	IgM (mg/dL)	87.7	35–220
Platelet ($\times 10^4$/μL)	13.9	15.5–35.0	C-reactive protein (mg/dL)	0.3	0.0–0.3
Prothrombin time (%)	83.1	≧75	C3 (mg/dL)	25	86–160
Activated partial thromboplastin time (sec)	39.1	27.0–40.0	C4 (mg/dL)	2	17–45
Total protein (g/dL)	5.0	6.9–8.4	CH_{50} (U/mL)	7	30–50
Albumin (g/dL)	2.2	3.9–5.2	C1q (μg/mL)	14.9	≦3.0
Aspartate aminotransferase (IU/L)	29	13–33	Rheumatoid factor (IU/mL)	27	0–15
Alanine aminotransferase (IU/L)	14	6–27	Antinuclear antibody	×640	< 40
Alkaline phosphatase (IU/L)	181	117–350	Anti-double strand DNA antibody (IU/mL)	3140	< 12
Lactate dehydrogenase (IU/L)	201	119–229	Anti-Sm antibody	Negative	Negative
γ-Glutamyl transpeptidase (IU/L)	68	9–109	Anti-RNP antibody	Negative	Negative
Total bilirubin (mg/dL)	0.7	0.3–1.1	Anti-SS-A antibody	16	Negative
Cholinesterase (IU/L)	160	220–495	Anti-smooth muscle antibody	Negative	Negative
NH_3 (μg/dL)	79	6–51	Anti-liver/kidney microsome type 1 antibody	Negative	Negative
Urea nitrogen (mg/dL)	62	8–21	Anti-mitochondrial M_2 antibody (U/mL)	2.9	< 7.0
Creatinine (mg/dL)	1.47	0.46–0.78	Hepatitis B virus DNA	Negative	Negative
Uric acid (mg/dL)	8.7	2.5–7.0	Hepatitis C virus RNA	Negative	Negative
eGFR (mL/min/1.73 m^2)	27.6	≧90	Urinary RBC sediment (/HPF)	11–30	< 1
Na (mmol/L)	141	139–146	Urinary protein (g/day)	6.52	< 0.15
K (mmol/L)	4.8	3.7–4.8			
Cl (mmol/L)	113	101–109			

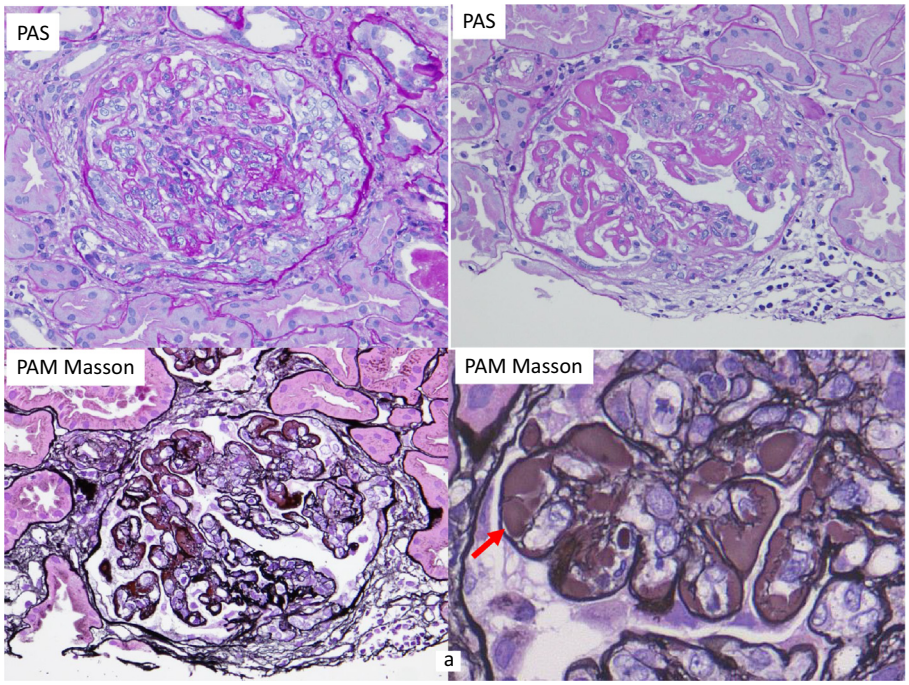

Fig. 1. Microscopy of a renal biopsy specimen. a: Extracapillary and endocapillary glomerulonephritis is noted. In glomeruli with few or no proliferative changes, the peripheral intracapillary spaces are markedly widened and filled with homogenous and rigid material (arrow) on PAM-Masson staining, forming so-called "wire loop" lesions. b: Immunofluorescence (IF) shows prominent deposits of IgG, IgA, IgM, C3, and C1q (full house) within the glomerular basement membrane and the mesangial region. c: On electron microscopy (EM), massive subendothelial electron-dense deposits (EDD) are noted, but there are no microfibrillary structures showing a fingerprint pattern (inset).

Thereafter, she was stable without immunosuppressant therapy. Six months before admission, her creatinine was 0.68 mg/dL and her estimated glomerular filtration rate (eGFR) was 64.1 mL/min/1.73 m^2, but creatinine began to increase subsequently and anasarca became severe.

On admission, she had a height of 153.5 cm and weight of 63.9 kg (weight gain of 7.6 kg in 1 month), with a blood pressure of 133/54 mmHg, heart rate of 78/min, and temperature of 37.2 °C. There was severe edema of the legs, and oral ulceration was detected. However, there were no other skin lesions, and no joint pain or neurologic symptoms. Laboratory findings were as follows (Table 1): white blood cell count, 3800/μL; red blood cell count, 2.99 × 10^6/μL; hemoglobin, 9.6 g/dL; platelet count, 139 × 10^3/μL; total protein, 5.0 g/dL; albumin, 2.2 g/dL; serum urea nitrogen, 62 mg/dL; serum creatinine, 1.47 mg/dL; eGFR, 27.6 mL/min/1.73 m^2, and CRP was 0.3 mg/dL. Immunological studies were positive for speckled and homogenous antinuclear antibody. In addition, anti-double-stranded DNA (anti-ds-DNA) antibody was 3140 IU/mL (normal: > 12) and anti-SS-A (Ro) antibodies were positive at a titer of 1:16. However, anti-U1 ribonucleoprotein antibody and anti-Smith antibody were negative. Antiphospholipid antibody was also negative, including anti-cardiolipin