

The Relevance between Renal Ultrasonographic Findings and Disease Course in Two Poststreptococcal Glomerulonephritis (PSGN) Patients

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Poststreptococcal glomerulonephritis (PSGN) is one of the most well-known and important infectious renal diseases resulting from a prior infection with group A β -hemolytic streptococcus. The typical clinical characteristics of the disease reflect acute onset with gross hematuria, edema, hypertension and moderate proteinuria after the antecedent streptococcal infection. In children, usually PSGN is healed spontaneously but if it combines with fast progressing glomerulonephritis, it would be developed to chronic renal failure. Therefore, it is important to make a fast diagnosis and treatment by simple tools to predict the course and the prognosis of disease. Sonography is a simple tool for diagnosis but there is no typical renal sonographic finding in PSGN, so it is difficult to predict the course and the prognosis of disease by sonographic findings. In comparison between two cases of renal sonographic findings in PSGN, a patient who showed more increased echogenicity in more extended area of renal sonography had the severe results of renal pathology, prolonged treatment period and low serum C3 level. Here, we report the different findings of renal sonography and pathology depending on the degree of severity between two patients. Thus, it is necessary to gather more information from further studies to make a consensus about the relationship between the renal sonography and the prognosis of disease in PSGN.

Key words: Glomerulonephritis, Streptococcal infections, Renal sonography

Introduction

Poststreptococcal glomerulonephritis (PSGN) is an immunologically mediated glomerular injury triggered by streptococcal infections. PSGN usually occurs in children and there are differences in the prognosis between children and adults¹. PSGN is a self-limited disease, especially in children and young adults, and they show good prognosis²⁻⁴. In contrast, PSGN is more likely to progress to renal failure in elderly adults. Over 90% of patients have hematuria and few patients show nephrotic range proteinuria. If rapidly progressive glomerulonephritis is rarely combined, about 50% of patients progress to chronic renal failure. If nephrotic range proteinuria is presented, the prognosis is poor, so it is important to get primary fast treatment to have the good prognosis^{3,5}. In PSGN, elevated antistreptolysin O (ASO) titers and



Fig. 1. The findings of renal sonography in case 1 and case 2. (A) Sonographic findings of case 1. There was markedly increased echogenicity from central renal sinus to cortex. (B) Sonographic findings of case 2. Increased echogenicity was found in only central renal sinus. (C) Sonographic findings of case 1 after 2 months. Increased echogenicity was still showed in renal sinus, but decreased echogenicity was showed in cortex.

decreased complement 3 (C3) are typical findings. Subepithelial hump is the characteristic in biopsies, and C3 and Immunoglobulin G (IgG) are staining in immunofluorescence microscopy (IF). The patterns of renal sonography are nonspecific. Thus we report the different findings of renal sonography and pathology between two patients with PSGN.

Case report

1. Case 1

A 5 years old boy, previously in a good health, was admitted with bloody and foamy urine for a week. One week prior to admission, the patient had a sore throat but no fever. He had received oral antibiotics for a day. He didn't have any family history of kidney disease. He didn't have facial swelling, generalized edema, a pale face and petechiae on upper and lower extremities. His height was 120 cm (>97th percentile) and body weight was 23 kg (50-75th percentile) with a blood pressure of 135/95 mmHg (>99th percentile).

Laboratory findings at serum were: hemoglobin, 10.3 g/dL; white blood cell, 10,850/mm³, with 55.8% segmented neutrophils, 31.2% lymphocytes; platelet count, 309,000/mm³; total protein, 6.8 g/dL; albumin, 3.2 g/dL; BUN, 25.6 mg/dL; creatinine, 0.87 mg/dL; calcium, 8.4 mg/dL; phosphorus, 5.0 mg/dL; total cholesterol, 170 mg/dL; LDL-cholesterol, 104 mg/dL; HDL-cholesterol, 42 mg/dL. The result of coagulation test was normal (PT INR 1.03, aPTT 39.2sec). The ASO titer was 2,140 IU/mL (normal

0~166 IU/mL). C3 was below 11mg/dL (normal 86-160 mg/dL), C4 was 10.0 mg/dL (normal 17-47 mg/dL) and complement hemolysis 50 (CH50) was below 2u/mL (normal 23.0-46.0). The serums IgG, IgA and IgM were 2,017.0 mg/dL, 198 mg/dL, and 96.0 mg/dL, respectively. Antineutrophil cytoplasmic antibody (ANCA) was weakly positive. Anti-dsDNA, LE cell and coombs test were negative.

Urinalysis revealed: specific gravity, 1.020; PH, 5.0; protein, 3+; occult blood, 3+; red blood cells(RBC), >100/high-power field (HPF). The urine chemistry showed proteinuria at 4,938.9 mg/24 hrs, and creatinine at 32.66 mg/24 hrs. Urine culture was negative.

In renal sonography, prominently increased echogenicity was showed from renal sinus to cortex in both kidneys (Fig. 1A).

The kidney biopsy was done due to persisting gross hematuria for more than 10 days. Under light microscopy evaluation, the kidney biopsy specimen showed glomeruli which were markedly increased size and severely hypercellular involving endocapillary and mesangial cells. Four of glomeruli showed global sclerosis and there were no urinary spaces. The tubules reveal focal moderate atrophy and loss with infiltration of mononuclear cells in edematous interstitium (Fig. 2A). Immunofluorescent studies showed diffuse glomerular staining for C3 and IgG (Fig. 2C and E). Under electron microscopy (EM) examination, there were dome-shaped subepithelial electron dense deposits ("humps"), and small amounts of subendothelial and mesangial deposits (Fig. 2G). Two months after discharge, the serum C3 and C4 were still low (67 mg/dL and 13 mg/dL, respectively),

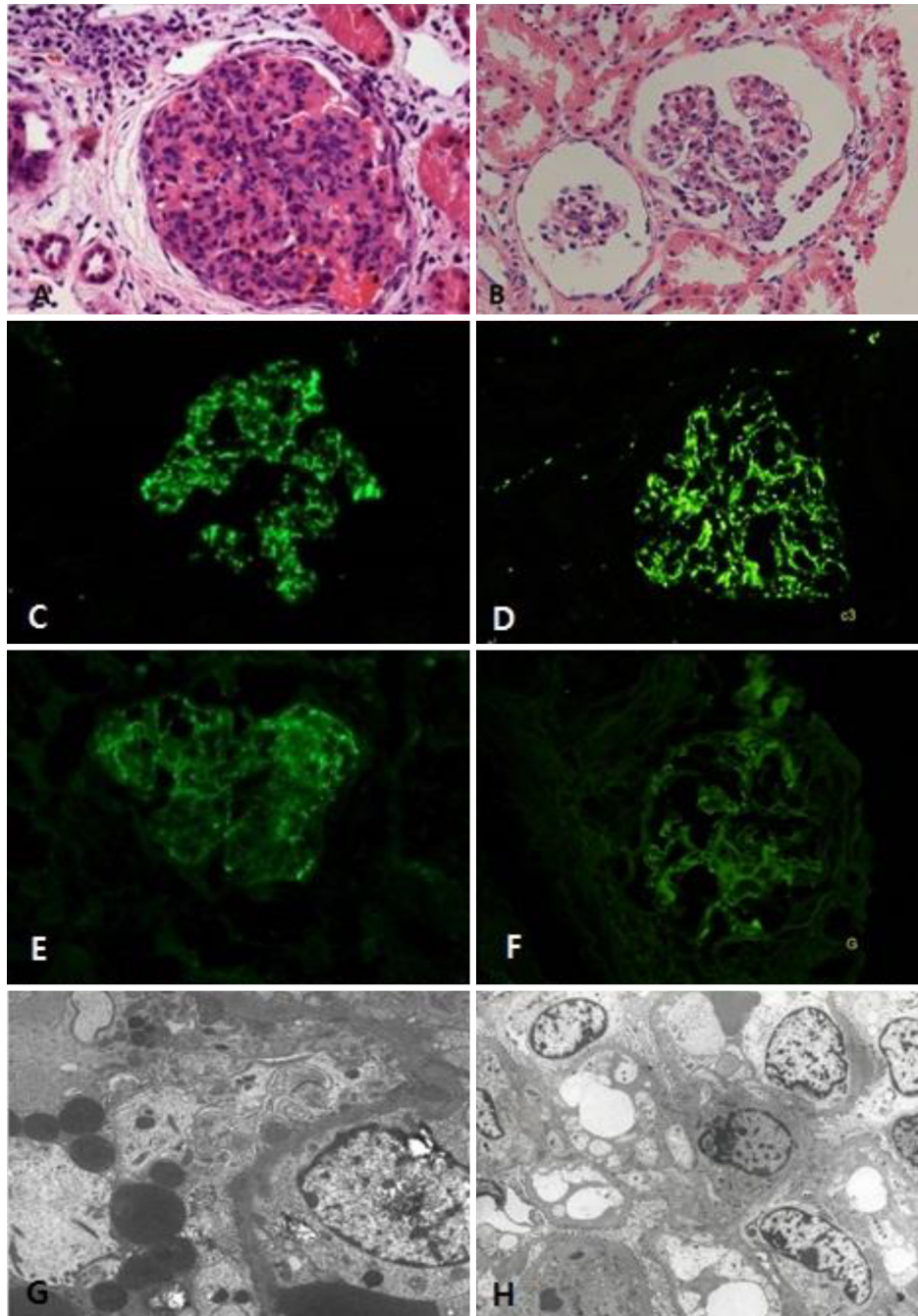


Fig. 2. Renal histologic, IF and EM findings in case 1 and case 2. (A) Light microscopic examination of case 1 ($\times 400$). Some glomerulus shows global sclerosis. The remaining glomeruli are of markedly increased size and severely hypercellular involving endocapillary and mesangial cells. There are no urinary spaces. (B) Light microscopic examination of case 2 ($\times 400$). The glomeruli show mild increase in size and cellularity. Tubules, interstitium and blood vessels are unremarkable under hematoxylin-eosin staining. (C and E) Immunofluorescence staining of case 1 (C3 and IgG, $\times 400$). There is a diffuse granular peripheral staining of IgG and C3. (D and F) Immunofluorescence staining of case 2 (C3 and IgG, $\times 400$). C3 reveals diffuse and strong staining in the mesangium and capillary wall whereas IgG is completely negative even in the repeat stains. (G) Electron microscopic examination of case 1 ($\times 2500$, scale bar = 200 nm). Scattered but numerous subepithelial humps and small amounts of subendothelial and mesangial deposits are seen. (H) Electron microscopic examination of case 2 ($\times 2500$, scale bar = 200 nm). Frequent intramembranous, subepithelial and mesangial electron dense deposits are seen with occasionally subepithelial hump like deposit (arrow).

Table 1. Comparison of laboratory findings and urinalysis between case 1 and case 2

	Case 1			Case 2	
	Initial	2month later	5month later	Initial	2month later
ASO(IU/mL)	2,140			1,160	
C3(mg/dL)	11	67	110	<26	110
C4(mg/dL)	10.0	13	21	30.2	19.2
CH50(u/mL)	<2	32.6		<3-6	16.4
IgG(mg/dL)	2017.0			1651	
IgA(mg/dL)	198			194	
IgM(mg/dL)	96.0			103	
ANCA	Weakly positive			Positive	
Anti-dsDNA	Negative			Negative	
LE cell	Negative			Negative	
Coombs test	Negative			Negative	
Urinalysis					
Specific gravity	1.020	1.020		1.010	1.015
PH	5.0	5.5		8.5	7.0
Protein	3+	Negative	Trace	2+	Negative
Blood	3+	3+	2+	3+	1+
Red blood cells/HPF	>100	5-9	1-4	>100	5-9
Urine Cx.	Negative			Negative	

but serum CH50 were improved (32.6 u/ml). Urinalysis revealed: specific gravity, 1.020; PH, 5.5; protein, negative; occult blood, 3+; red blood cells (RBC), 5-9/HPF. Also, a large number of dysmorphic red blood cells were showed on microscopic examination. In follow up renal sonography, previous increased echogenicity was still showed in renal sinus, but decreased echogenicity was observed in cortex (Fig. 1C).

Five months after initial diagnosis with continuous conservative treatment, serum C3 and C4 were normalized (110 mg/dL, 21 mg/dL, respectively). The Urine was positive for occult blood (2+), protein (trace), and red blood cells (RBC) were a few (1-4/HPF) (Table 1).

2. Case 2

A 5 years old boy presented with bloody urine for a week to urology department. The renal ultrasound suggested the presence of renal parenchymal disease. He was transferred to the pediatric department for a renal biopsy to differentiate from glomerulonephritis. He didn't have any family history of kidney disease, any sign of nephrotic syndrome and no recent infectious sign. His height was 109cm (10-25th percentile) and body weight was 17 kg (10-

25th percentile) with a blood pressure of 130/80 mmHg (>99th percentile).

Laboratory findings at serum were: hemoglobin, 12.6 g/dL; white blood cell, 8,300/mm³, with 66.7% segmented neutrophils, 24% lymphocytes; platelet, 347,000/mm³; total protein, 7.5 g/dL; albumin, 4.6 g/dL; BUN, 10.5 mg/dL; creatinine, 0.6 mg/dL; calcium, 9.5 mg/dL; phosphorus, 4.8 mg/dL; total cholesterol, 146 mg/dL; LDL-cholesterol, 84 mg/dL; HDL-cholesterol, 45 mg/dL. The titer of ASO was 1,160 IU/mL (normal 0~166 IU/mL). Serum C3 was below 26 mg/dL (normal 86-160 mg/dL), C4 was 30.2 mg/dL (normal 17-47 mg/dL) and CH50 was below 3-6 u/mL (normal 23.0-46.0). The serum IgG, IgA, and IgM were 1,651 mg/dL, 194 mg/dL, and 103 mg/dL, respectively. ANCA was positive. Anti-dsDNA, LE cell and coombs test were negative.

Urinalysis revealed: specific gravity, 1.010; PH, 8.5; occult blood, 3+; protein, 2+; red blood cells(RBC), >100/HPF. The urine chemistry showed proteinuria (224.9 mg/24 hr), and creatinine (321.1 mg/24 hr). Urine culture was negative.

The sonogram of both kidney demonstrated increased cortical echogenicity and reduction in renal sinus echogenicity (Fig. 1B).

The kidney biopsy was done at 6 days after first gross hematuria. Under light microscopic evaluation, the glomeruli showed mild increase in size and moderate hypercellularity with mesangial and endocapillary proliferation (Fig. 2B). Under IF, C3 staining was seen in mesangial and capillary wall, but IgG was not highlighted (Fig. 2D and F). Electron microscopy findings demonstrated the characteristic of subepithelial “humps” (Fig. 2H).

Two months after initial diagnosis with continuous conservative treatment, the serum C3 and C4 were normal (110 mg/dL and 19.2 mg/dL, respectively), and serum CH50 were also improved (16.1u/ml). Urinalysis showed a specific gravity of 1.015, a PH of 7.0. The urine was negative for protein. The urine was positive for blood (1+), and red blood cells (RBC) were a few (5-9/HPF) (Table 1).

Discussion

PSGN may be a consequence of streptococcal pharyngitis or pyoderma, and it is the most common form of immune-mediated nephritis in children. Gross hematuria, proteinuria, hypertension and edema are the classic manifestations³. PSGN occurs usually in children, and it could be healed by conservative treatment. Most PSGN patients, especially children, have good prognosis⁶. However, some patients, especially adults, with hypertension, and persistent proteinuria develop chronic renal failure 10~40 years after PSGN⁷. Usually, PSGN would be diagnosed by history of prior streptococcal infection, urinalysis, and serum complement test. In renal sonography, increased cortex echogenicity could be showed, which could be presented in renal parenchymal diseases such as acute glomerulonephritis, pyelonephritis and nephrotic syndrome, so it is not specific to make a diagnosis or predict prognosis. If a patient presents severe clinical manifestations such as prolonged hematuria and proteinuria more than 6-8wks, low C3 level which persist more than 2 months, renal biopsy should be considered.

Typical renal biopsy findings in PSGN show diffuse endocapillary and glomerular hypercellularity and subepithelial hump. Immunofluorescence (IF) microscopy highlights granular deposits with C3 and Ig G⁸.

Most patients of PSGN (about 90%) have decreased levels of serum C3 and minimally depressed or normal levels of

serum C4. Complement levels usually return to normal within 4 to 6 weeks. From Kasap et al.⁹, the findings of renal sonography are related to renal functions and clinical severity of disease. Tubular atrophy and interstitial inflammation are correlated with renal cortical echogenicity. Possible mechanisms by tubular atrophy which could increase renal cortical echogenicity include thickening of the renal tubular basement membranes or luminal dilatation of remaining tubules. Our data indicated that diffuse increased echogenicity of renal parenchyma is associated with not only prolonged duration of gross hematuria and decreased serum C3 level but also severe renal histologic changes. Increased renal cortical echogenicity was graded according to the following standard classification: grade I, renal cortex and liver equally echogenic; grade II, renal cortex more echogenic than liver; grade III, renal cortex and sinus equally echogenic¹⁰. In case 1, increased renal echogenicity was classified into grade III and extended from renal sinus to cortex in both kidney. In case 2, increased cortical echogenicity was classified into grade I and renal sinus echogenicity is reduced. In renal pathology, it showed more sclerosis region and narrowed urinary space in case 1 than in case 2. It took five months that serum C3 and C4 were normalized in the first patient, but it took only two months that they were normalized in the second patient. This result may reflect that the severity of disease could be related to the results of renal ultrasonography.

In Korea, few studies have been reported about the association between renal sonography and prognosis. From comparison between these two cases, if the extended and increased echogenicity of renal parenchyma is seen in sonography, it may be helpful to predict the severity and prognosis of the disease. Therefore, patients could be treated earlier. Although, the first patient who showed more increased and extended echogenicity had conservative treatment, we paid attention and followed up carefully. However, the association between renal sonography and prognosis has not been established, so it is necessary to gather more information from further studies to make a consensus about this association.

Progression of renal disease must be monitored closely to predict prognosis and make proper treatment plan. Usually, renal biopsy is a popular diagnostic tool, but it is invasive and time consuming. Therefore, if ultrasound is

used to make a diagnosis and predict prognosis, it will be more secure and convenient than renal biopsy.

In conclusion, the degree of increased renal cortical echogenicity reflects clinical phase, prolonged treatment duration, decreased C3 level and histologic changes.

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