

Acute Post-streptococcal Glomerulonephritis with Normal Range Complement C3 Level: Three Case Reports

GL QIAN, L HUANG, JH MAO, AM LIU

Abstract

Introduction: Acute post-streptococcal glomerulonephritis (APSGN) is a common disease that primarily affects children. At the acute phase of post-streptococcal glomerulonephritis, the level of haemolytic complement plasma C3 always decreases. The hypocomplementaemia is one of the important criteria for diagnosis of APSGN. We identified 3 children with acute post-streptococcal glomerulonephritis diagnosed clinically and pathologically whose plasma C3 levels remained normal range in the acute phase. **Case presentation:** All of the three patients are Chinese (a 5.8-year-old boy, a 8.8-year-old girl, and a 6.9-year-old girl). Their plasma C3 levels were 0.99 g/L, 0.64 g/L, and 0.66 g/L (normal range: 0.5-1.5 g/L) in the acute phase. Pathological findings showed that subepithelial hump-like dense deposits were present. **Conclusion:** It is possible for patients with APSGN that serum complement C3 level remains normal range during acute phase. Even if plasma C3 levels are still normal, the possibility of acute post-streptococcal glomerulonephritis cannot be ignored. Renal biopsy and follow-up of C3 level variation will be necessary for definite diagnosis of these patients.

Key words

Acute post-streptococcal glomerulonephritis; Haemolytic complement plasma C3; Kidney biopsy

Introduction

Acute post-streptococcal glomerulonephritis (APSGN) is a common form of kidney disease. In the acute phase of this disease, haemolytic complement plasma C3 levels always decrease, but these levels usually return to normal within 8 weeks.¹ The hypocomplementaemia is an

important criterion for diagnosis of APSGN. But during the past 2 years, 78 patients admitted to our department with acute post-streptococcal glomerulonephritis. Among them, three patients presented with normal plasma C3 levels (3.85%). This phenomenon results in an uncertain diagnosis. We report these 3 cases below.

Case Presentation

Case 1

A 5.8-year-old boy was admitted our hospital because of oedema on both of his eyelids accompanied by a change in urine color for 2 weeks. He had a cold 1 week ago. A urine test showed that red blood cells (RBC) were +++, proteinuria was +++. On the 5th day since the symptoms appeared. He then came to our hospital and had a physical examination, which showed a blood pressure (BP) of 93/55 mmHg, his weight was 17.5 kg, and both his eyelids had oedema. The C3 level was 0.99 g/L (0.6-1.5 g/L) on the 5th day from the disease, which turned to 1.34 g/L (0.5-1.5 g/L) on the 14th day. Antistreptolysin O test (ASO)

Nephrology Ward, Children's Hospital, Zhejiang University School of Medicine, 57 ZhuganXiang, Hangzhou, 310003, China

L HUANG (黃雷) MD
HJ MAO (毛建華) PhD
AM LIU (劉愛民) PhD

Department of Genetics and Metabolism, Children's Hospital, Zhejiang University School of Medicine, 57 ZhuganXiang, Hangzhou, 310003, China

GL QIAN (錢古矜) MD

Correspondence to: Dr L HUANG

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was 15 U/mL (0-200 U/mL), and the erythrocyte sedimentation rate (ESR) was 46 mm/h (0-20 mm/h). A biochemistry test showed that the level of albumin was 35 g/L, alanine aminotransferase (ALT) was 9 U/L, creatinine was 55.5 μ mol/L, urea was 7.04 mmol/L, and triglycerides were 1.87 mmol/L. The 24-hr urinary protein excretion was 1.5 g/24 hr (85.7 mg/kg/day). B-Ultrasound showed diffuse enlargement on the kidney. Results for antinuclear antibody (ANA), hepatitis B, and hepatitis C were negative. Tuberculosis was negative. A renal biopsy showed endothelial and mesangial cell proliferation. Immunofluorescence immune depositions C3+++ in the mesangial area and capillary loops. Electron microscopy showed that subepithelial hump-like dense deposits were found under epithelial cells. Renal biopsy results suggested endocapillary proliferative glomerulonephritis (Figure 1). We diagnosed the patient with acute post-streptococcal glomerulonephritis. For treatment and prognosis, he rested in bed and was given diuretic furosemide, ampicillin for infection, and benazepril for low BP. His urine output had increased to 1000 ml in 2 days after admission. He was then discharged, and at that time, his proteinuria was ++ and RBC count in urine was >200/HF. He was not given any medication. After 1 month, he came back, his proteinuria became normal. Currently, his RBC count in urine is normal.

Case 2

A 8.8-year-old girl was admitted our hospital because of oedema for 3 days and oliguria for half a day. Five days before her admission, there were some rashes on her legs and she felt throat pain. On the second day since the symptoms appeared, she was taken to a local hospital. Tests showed the following: urine dipstick tests RBC+++, proteinuria +++++, BP was 110/80 mmHg, the creatinine level was 201 μ mol/L, and the blood urea nitrogen level was 16.7 mmol/L. She was then admitted to the emergency room in our hospital. At this time, serum creatinine was 423 μ mol/L and blood urea nitrogen was 9.74 mmol/L. She came to our ward and had a physical examination, which showed that her BP was 100/58 mmHg, her weight was 28 kg, her face and both eyelids had oedema, there were some old red rashes on her legs. The C3 level was 0.64 g/L (0.5-1.5 g/L) on the 3rd day from the disease, it was 1.29 g/L on the 11th day, and it was 1.14 g/L on 4 weeks later. ASO was 1207 U/mL (0-200 U/mL), and the ESR was 24 mm/h. A biochemistry test showed that the level of albumin was 26.1 g/L, creatinine was 363.7 μ mol/L, and urea was 23.12 mmol/L. The 24-hr urinary protein excretion

was 2.019 g/24 hr. B-Ultrasound showed diffuse enlargement on the kidney. ANA, hepatitis B, and hepatitis C were negative. And tuberculosis antibody was negative. A renal biopsy also showed mesangial and endothelial cells proliferations. Immunofluorescence showed immune depositions C3+++ in the mesangial area and capillary loops. Electron microscopy showed subepithelial hump-like dense deposits were observed under epithelial cells. Renal biopsy results suggested endocapillary proliferative glomerulonephritis (Figure 2). The diagnosis was acute post-streptococcal glomerulonephritis. For treatment and prognosis, the patient had rested in bed and was given diuretic furosemide, ampicillin for infection, and a short period of prednisone (1 mg/kg/d for 10 d). When he was discharged, his proteinuria was ++ and RBC in urine were 197/HP. After discharge, he took Chinese medicine. One month later, he came back to the hospital and a checkup showed that his proteinuria was normal. Six months later, RBC in urine were also at normal levels.

Case 3

A 6.9-year-old girl was admitted our hospital because of oedema for 6 days and oliguria for 2 days. On the 3rd day since the symptoms appeared, she was taken to a local hospital. Tests showed that the urine RBC count was 147/HF, proteinuria was +++++, the C3 level was 0.74 g/L (0.7-1.5 g/L), the serum creatinine level was 325 μ mol/L, and blood urea nitrogen level was 33.1 mmol/L. Physical examination during administration to our hospital showed a BP of 106/77 mmHg, her weight was 22 kg, both of her eyelids and her legs had oedema, which is non-pitting. The C3 level was 0.66 g/L (0.5-1.5 g/L) on the 6th day from the disease, and it was 0.81 g/L (0.5-1.5 g/L) on the 13th day. ASO was 662 U/mL (0-200 U/mL), Hb was 86 g/L, and the ESR was 27 mm/h. A biochemistry test showed that the level of albumin was 22.4 g/L, ALT was 7 U/L, creatinine was 281.1 μ mol/L, urea was 32.2 mmol/L, and triglycerides were 2.48 mmol/L. 24-hr urinary protein excretion was 1.67 g/24 h (77.5 mg/m²/hr). A routine urine test showed urine protein +++++ and RBC in urine were >200/HP. B-Ultrasound showed diffuse enlargement on the kidney. ANA, hepatitis B, and hepatitis C were negative. Tuberculosis were negative. Renal biopsy also suggested endocapillary proliferative glomerulonephritis. The diagnosis was acute post-streptococcal glomerulonephritis. For treatment and prognosis, the patient rested in bed and was given diuretic furosemide and furbucilin for infection. She had increased urine output for 3 days after admission, and creatinine and blood urea nitrogen levels were

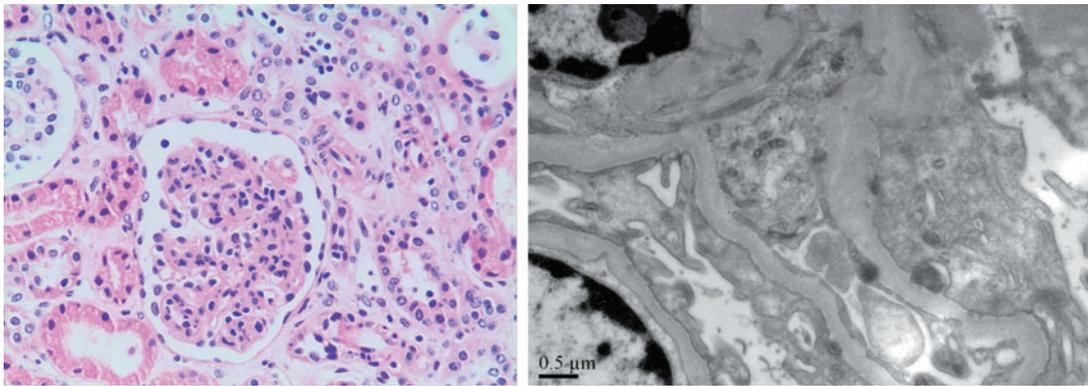


Figure 1 Kidney biopsy of case 1 (left: H&E x 200; right: electron microscopy x 25000).

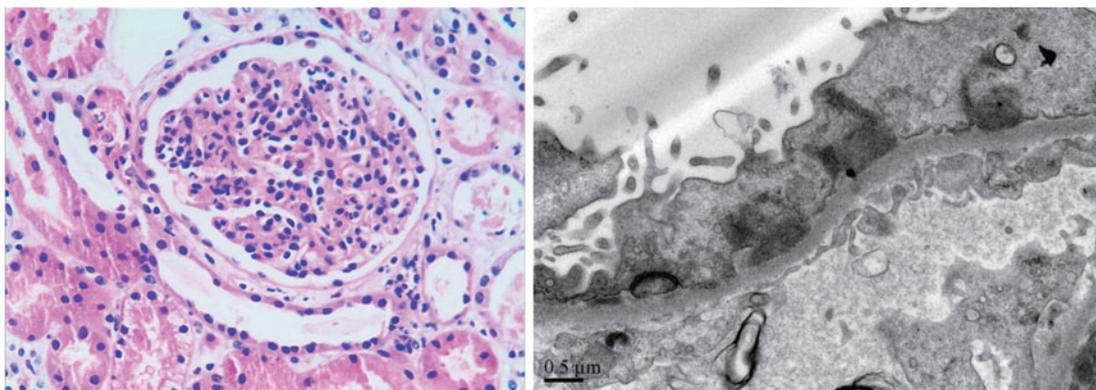


Figure 2 Kidney biopsy of case 2 (left: H&E x 200; right: electron microscopy x 25000).

decreased. However, proteinuria was still not in remission. On the fifteenth day after her admission, we misdiagnosed her as having nephrotic syndrome, and gave prednisone for treatment. Shortly after that, kidney biopsy results showed that we had made an incorrect diagnosis, and we stopped prednisone. We still required the patient to rest and she was treated with heteropathy. She was discharged when gross haematuria disappeared. After being discharged, she was treated with Piperazine Ferulate and ferralia. After 2 months, she came to our hospital and had a checkup, and we found that her proteinuria was normal. Her Hb levels were normal 3 months later. Six months later, RBC in urine was at normal levels.

Discussion

In the past 2 years, a total of 78 patients were admitted to our department with APSGN. We found that 3 of those patients had normal plasma C3 levels. Pathological findings showed that subepithelial hump-like dense deposits were

present. Light microscopy showed endothelial cells proliferations. Physical examination and other test results excluded Henoch Schönlein purpura, lupus nephritis, and IgA nephropathy. And now the three patients all have recovered with only symptomatic treatment, which indicated that our diagnosis was definite. During the clinical period, cases 2 and 3 had acute kidney injury, and case 3 was misdiagnosed with nephrotic syndrome because of the high proteinuria level and hypoalbuminaemia. Previous reports also indicate that there are some patients suffering with acute post-streptococcal glomerulonephritis have normal plasma C3 levels. Through a four-year prospective clinical study of the acute episode in APSGN, Khuffash et al² found the C3 level was low in 97 percent of all the 187 paediatric patients. Leung et al³ studied 74 paediatric patients with APSGN, and they found serum C3 concentration was low in 73 patients. Shroff et al⁴ reported C3 was found to be low in 88 percent of the patients at the onset of illness in the APSGN group which including 62 patients, and all the patients had kidney biopsy.

In fact, other infectious agents can also cause acute

glomerulonephritis, so the diagnosis can be broader to be called post-infectious glomerulo-nephritis. Normal C3 has been well described in some 10% of such patients. We need to notice this during our clinical work.

Welch⁵ said in his article that the importance of a timely measurement of C3 cannot be overstressed in APSGN because the hypocomplementaemia is evanescent, typically normalising in six to eight weeks. But the first plasma C3 levels of these three patients were gotten at the fifth day, third day, sixth day from the symptoms, the time points seemed to be suitable, and they were all in the normal range. Thus, the importance of a timely measurement of C3 cannot be overstressed not only because of the hypocomplementaemia is evanescent but also the C3 level will not always decrease absolutely.

We currently believe that the pathogenesis of APSGN is due to multi streptococcal antigen and a host antibody response to the formation of soluble complexes, which cannot be removed by the glomeruli and activate the complement system. Some studies^{6,7} indicate that an alternative pathway of complement activity is the most important prognosis of APSGN. We also observed strong endocapillary deposit of C3 shown by immunofluorescence, suggesting that an alternative complement pathway is involved in the leading cause of morbidity. Further studies are required to determine why acute phase C3 levels still remained within the normal range.

In short, even if plasma C3 levels are still normal, the possibility of acute post-streptococcal glomerulonephritis cannot be ignored. We should alert to this phenomena in order to avoid misdiagnosis and the side effects of unnecessary treatments.

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Declaration of Interest

We declare no potential conflicts of interest involved in this article.

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