

Case Report

Diffuse mesangial and endocapillary cell proliferative glomerulonephritis with persistent hypocomplementemia in a child

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Abstract: A 15-year-old boy was admitted to People's Hospital of Dong E with anasarca. The laboratory findings revealed proteinuria, hematuria, hypocomplementemia. Renal biopsy specimen revealed diffuse mesangial and endocapillary cell proliferative glomerulonephritis on light microscopic (LM) examination. On immunofluorescence (IF) examination, deposition of IgG, IgA, C3, C1q and F to capillary wall and subendothelial were observed. By means of electron microscopy (EM), subendothelial electron-dense deposits and segmental fusion of epithelial cell foot process were recognized. He was treated by only some supportive drugs, no ACEI/ARB, without glucocorticoids and immunosuppressive agents. About one month later, complete remission of proteinuria occurred. During next 62-weeks follow up, urinary analysis always showed microscopic hematuria. However, it is interesting to note that the serum complement C3 and C4 levels remained persistently low.

Keywords: Acute glomerulonephritis, hypocomplementemia, mesangial and endocapillary proliferative glomerulonephritis

Introduction

Endocapillary proliferative glomerulonephritis is characterized of diffuse endocapillary and mesangial cell proliferate glomerulonephritis [1]. The classic presentation is of acute glomerulonephritis. Although the most common cause of acute glomerulonephritis is Group A β -hemolytic streptococcus, other infections by bacteria such as *Staphylococcus aureus* and *Streptococcus viridans*, viral infections (human parvovirus B19) [2], and parasitic infections often cause acute glomerulonephritis [3], which mainly occurs in children and youth. Infection in the upper respiratory tract is often seen 1-2 weeks prior to the onset. The total complement activity (CH50) in the serum, C3, C5, and properdin levels were found to be significantly lower in the majority of patients [4-7]. The C1q and C4 levels were found to be slightly lower than the average in about 10% patients. However, the serum complement component levels of these patients returned to normal within 8 weeks.

A 15-year-old boy who presented with proteinuria, hematuria and anasarca after upper respiratory infection was studied. However, his serum anti-streptolysin O (ASO) was negative. Renal biopsy showed endocapillary proliferative glomerulonephritis. He was treated using conventional drugs and piperazine ferulate dispersible tablets. About one month later, proteinuria complete remission. However, through the 62-weeks follow-up, serum complement C3 and C4 levels of the patient remain persistently low, and urine analysis showed that microscopic hematuria was present with no apparent changes. It was reported that persistent hypocomplementemia was found in membranoproliferative glomerulonephritis (MPGN) [8], Henoch-Schönlein purpura (HSP) [9] and fibrillary glomerulonephritis (FGN) [10]. Persistent hypocomplementemia with endocapillary proliferative glomerulonephritis has not been reported.

Case presentation

A 15-year-old boy without previous diseases or known renal diseases had an upper respiratory

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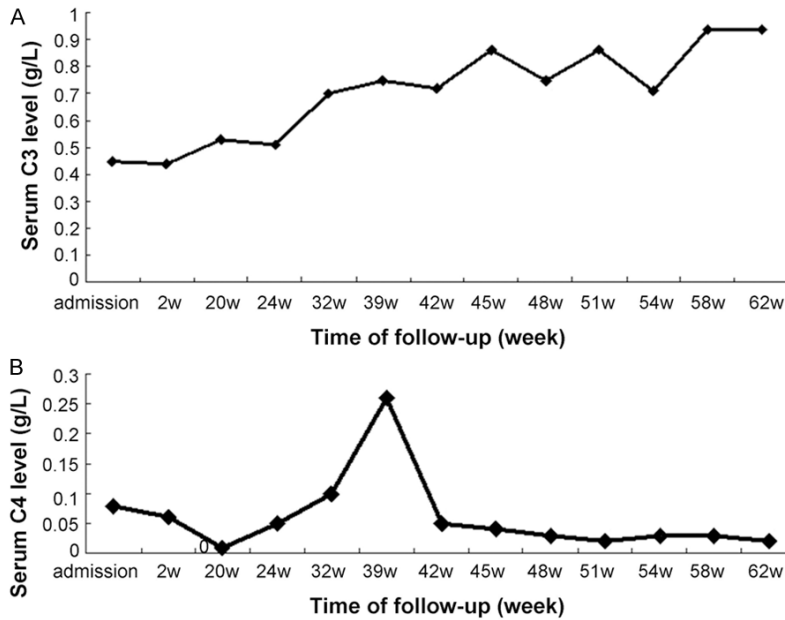


Figure 1. Evolution of serum C3 and C4 levels during 62-weeks following-up. A. The serum C3 level is slightly low at the early onset, it increases gradually and become normal at the 58th week of following-up. B. Detailed legend: The serum C4 level is slightly lower at the early onset, and it remains low across following-up.

tract infection in February 2013 with sore throat, cough, and tonsillar swelling without fever, and was treated with cephalosporin. One week later, he developed anasarca, without purpura and arthralgia. During physical examination, the blood pressure was found to be 125/75 mmHg. Urinary analysis revealed microscopic hematuria and proteinuria (24-h proteinuria is 3516 mg/4000 mL urine volume) with normal renal function (serum creatinine: 42 μ mol/L). Other laboratory findings were as follows: hemoglobin, 12.1 g/dL; white cell count, 6.26×10^9 /L; and platelet count, 246×10^9 /L. The serum total protein was 61.7 g/L and albumin, 32 g/L. The coagulation study was not altered. The ASO level was 0.1 IU/mL (normal < 200 IU/mL). ANA, anti-dsDNA, anti-rNP, anti-JO-1, anti-SCL-70, anti-Sm, anti-SSA, anti-SSB, and ANCA antibody levels were found to be negative. The IgG level was 10.03 g/L; IgA, 4.75 g/L (normal < 4.0 g/L); IgM, 2.11 g/L; the C3 level was low, 0.25 g/L (normal = 0.9-1.8 g/L); the C4 level was low, 0.08 g/L (normal = 0.1-0.4 g/L); RF, 5.8 IU/ml (normal < 20 IU/mL); and CRP, 0.1 mg/L (normal < 10 mg/L). The test results for HbsAg, and HCV, TP, and HIV antibodies were negative.

Abdominal ultrasound revealed normal kidneys. Renal biopsy was performed. Thirty-nine

glomeruli were analyzed by light microscopy. The following were observed: glomerular mesangial cells and endothelial cell hyperplasia, leukocyte infiltration, nuclear formation, Fuchsinophilic protein deposits in mesangial area, and one small crescent forms. Focal atrophy and granular degeneration of renal tubular epithelium were also observed. Lymph and mononuclear cell focal infiltrates in renal interstitial with interstitial fibrosis was also noticed. The small artery showed no obvious pathological changes. Immunofluorescence results were as follows: IgG++, IgA+, IgM-, C3+++ , C1q+++ , and F+. Ultrastructural study with electron microscopy showed the presence of mesangial cells and endothelial cell

hyperplasia, subcutaneous electron-dense deposit, and the segmental fusion of epithelial cell foot process.

As the patient presented with acute glomerulonephritis, treatment was initiated with conventional drugs and piperazine ferulate dispersible tablets (without glucocorticoids and immunosuppressive agents). Subsequently, we observed the progressive decrease of proteinuria that remitted completely about one month later. Urinalysis revealed that microscopic hematuria during the 62-weeks follow-up without aggravation. Interestingly, across 62-weeks follow-up, the level of C3 was found to gradually increase, at the 58th week, increase to 0.94 g/L (normal: 0.9-1.8 g/L), C4 levels further decreased to 0.02 g/L (normal: 0.1-0.4 g/L). The evolution of the disease across 62-weeks follow-up is shown in **Figure 1**. Pathology picture is shown in **Figures 2** and **3**.

Discussion

The preceding upper respiratory tract infection, hypocomplementemia, and endocapillary proliferative glomerulonephritis in a young patient suggested acute post streptococcal glomerulonephritis (PSGN). However his ASO titer was not

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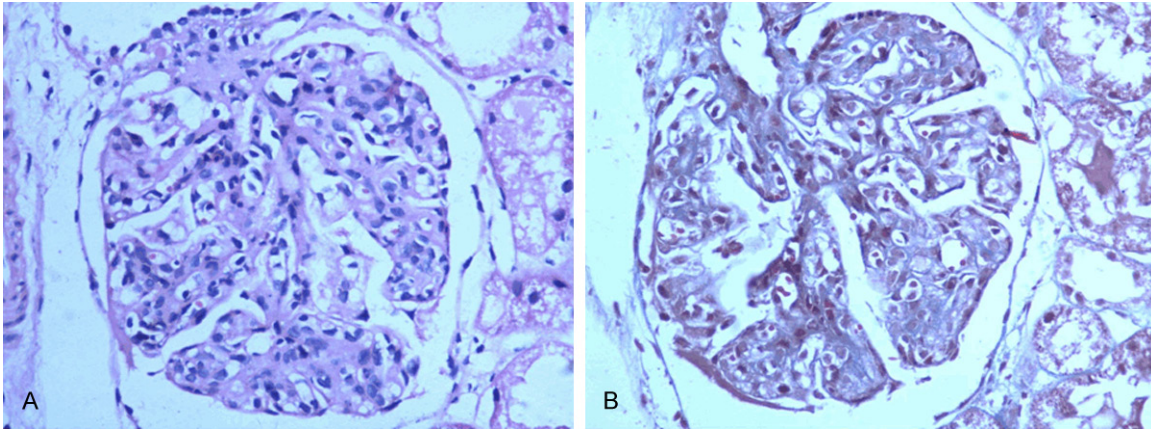


Figure 2. Pathology image of LM with different staining methods. A. H&E staining. Light microscopic observation of H&E staining shows diffuse mesangial and endocapillary proliferative glomerulonephritis and leukocyte infiltration. H&E: hematoxylin and eosin. B. Masson's staining. Fuchsinophilic protein deposited in the mesangial area.

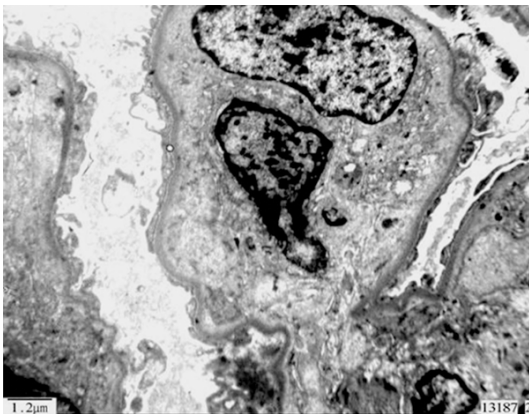


Figure 3. Pathology image of LM with Electron microscopy. Electron microscopy of the renal biopsy specimen reveals mesangial and endocapillary proliferation and subendothelial electron-dense deposits.

high. In EM, “the hump-shaped electron density,” which is a characteristic finding of PSGN [5], was not observed. In PSGN, CH50 and C3 levels are markedly low compared with C4 levels, however, the complement level has been reported to return to normal after less than 8 weeks in the regular course of PSGN [6, 7]. Initially, a moderate decrease in C3 and slightly low C4 in our patient were compatible with PSGN. While serum C3 and C4 levels were not completely normal after 1 year follow up in our patient. So, our case is an atypical of capillary proliferative glomerulonephritis. In recent years, many cases have shown the clinical manifestations mentioned below, indicating acute nephritis syndrome: endothelial cells

hyperplasia under the microscope; the immune pathological examination shows all are negative or only C3 is positive. In EM, the hump-shaped electron density cannot be found or only the mesangial area shows low electron density. After investigating its reason, some virus infection was considered as the cause [1]. Our case, combining with clinical course, the possibility of virus infection cannot be ruled out. But to the best of our knowledge, no literature reports state how the serum complement levels change and when they will return to normal in acute glomerulonephritis caused by virus.

Our patient was treated by only some supportive drugs, no ACEI/ARB, without glucocorticoids and immunosuppressive agents. The proteinuria completely remitted after one month. During the last one year, our patient only had microhaematuria as unique manifestation of renal disease without any aggravation. The serum C3 level gradually increased to normal at the 58th week. And C4 level still remain low. Therefore, in our case, the low C3 and C4 levels did not have any relation with the severity of renal evolution. Whether the hypocomplementemia is the result of complement activation after immunology activation from immune complex or indicates a congenital defect is difficult to clarify. In our case, the presence of low serum levels of C4, irrespective of clinical evolution, allows us to consider a congenital deficit because when nephropathy reached complete remission, the levels of serum C3 gradually increased to normal, but the levels of serum C4

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remained low. Indeed, the C4 congenital deficit is the most frequent complement congenital deficit, which in many occasions has no clinical consequences [9]. Defect in the complement system will increase the susceptibility to infection; especially when the classical pathway is affected, the disease manifested will be correlated with the immune system disorder. A significantly low C4 level and slightly decrease C3 level was observed in the patient, which is the conventional way to continue activating the complement system.

In summary, we met a patient who presented acute glomerulonephritis with persistent hypocomplementemia. And his pathology is diffuse mesangial and endocapillary cell proliferative glomerulonephritis. The low serum C3 and C4 levels did not have any relation with the severity of renal evolution. Serum C3 level gradually increased to normal, while serum C4 level still remain low at the 58th week during follow-up. We observed the evolution of complement C3 and C4 in one case. It may be helpful about the role of complement system on acute glomerulonephritis patient.

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Disclosure of conflict of interest

None.

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