

Original Article

Crescentic acute glomerulonephritis with isolated C3 deposition: a case report and review of literature

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Abstract: An eight-year-old girl, presenting with palpebral edema, gross hematuria, and foam in urine, was admitted to our hospital. Investigations indicated increased serum antistreptolysin O (ASO) and anti-mycoplasma antibody titers. Renal biopsy showed crescentic poststreptococcal acute glomerulonephritis (CPAGN) with isolated C3 deposition in the glomeruli. Electro-microscope examination showed subepithelial deposition of electron dense material. She received the double pulse therapies of methylprednisolone and cyclophosphamide as well as the treatment of oral prednisolone, angiotensin converting enzyme-II (ACE-II) inhibitor, dipyridamole and traditional Chinese medicine. The complete clinical remission was achieved after 9 months. No serious adverse effects were observed during the follow-up. Our findings indicated that CPAGN with isolated C3 deposition might have a favorable prognosis after aggressive immunosuppressive treatment. However, the influence of isolated C3 deposition on CPAGN prognosis remains to be clarified.

Keywords: Crescentic poststreptococcal acute glomerulonephritis, C3, deposition

Introduction

Complement, an important aspect of defense against infection, is activated and regulated finely [1]. Exclusive deposition of C3 at glomerular with an absence of immunoglobulin (Ig) deposits is due to the disordered complement regulation [2]. Studies of single cases and families has also identified key proteins which protect the kidney from complement-mediated damage [3]. Crescents, extracapillary hypercellularity with two or more layers of cells in Bowman space, are a sign of severe glomerular injury that can result from various causes and pathogenic mechanisms including infection [4]. The percentage of affected glomeruli is usually associated with the severity of kidney function and other clinical manifestations. Crescent formation is a complication of C3 glomerulonephritis (GN) [5]. However, crescentic poststreptococcal acute glomerulonephritis (CPAGN) associated with isolated C3 deposition is poorly documented in the literature. Most reported cases have no detailed natural history, medication and prognosis. The reports regarding Asian

patient with CPAGN with isolated C3 deposition was rare.

In this report, we described one girl who presented with clinical phenotype of CPAGN and whose initial renal biopsy was consistent with crescentic GN. Meanwhile, the IF showed the exclusive deposition of C3 in glomeruli. We also examined the clinicopathologic features and outcomes in this patient. The patient appeared to have a favorable prognosis.

Case report

An 8-year-old girl with 1-week of palpebral edema, gross hematuria, and foam in urine was admitted to our hospital. The urinalysis was normal and there were no episodes of hematuria prior to this hospitalization. She presented with no fever, diarrhea and headache. Physical examinations displayed normal blood pressure (106/70 mmHg), temperature (36.8°C) and pulse rate (87/min). Laboratory findings revealed anemia (hemoglobin 78 gm/L), normal serum levels of electrolytes, calcium and phosphate. Blood urea nitrogen was 10.26 mg/dl,

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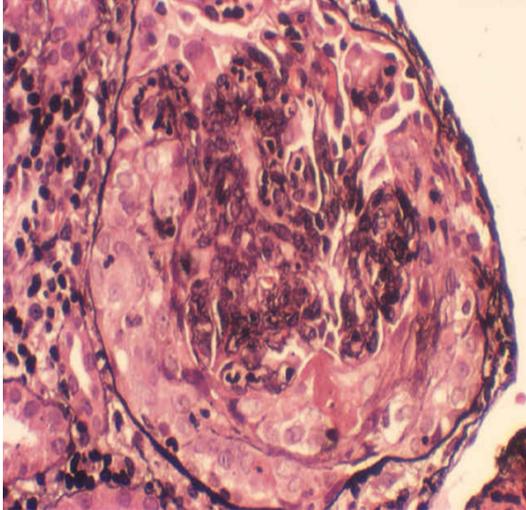


Figure 1. Glomeruli with endocapillary proliferation with cellular crescents (light microscopy, PAS staining).

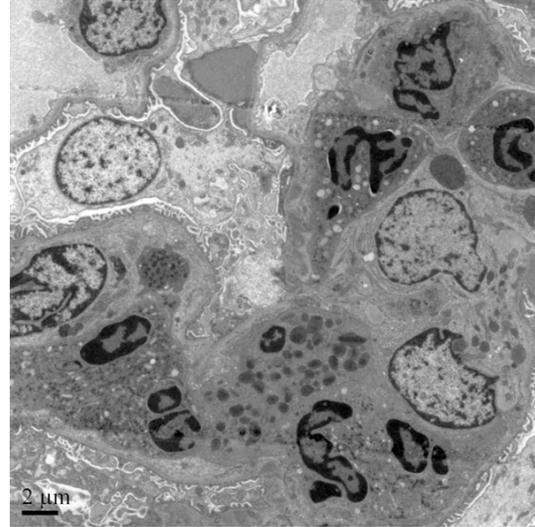


Figure 3. subepithelial deposition of electron dense material (Electro-microscopy).

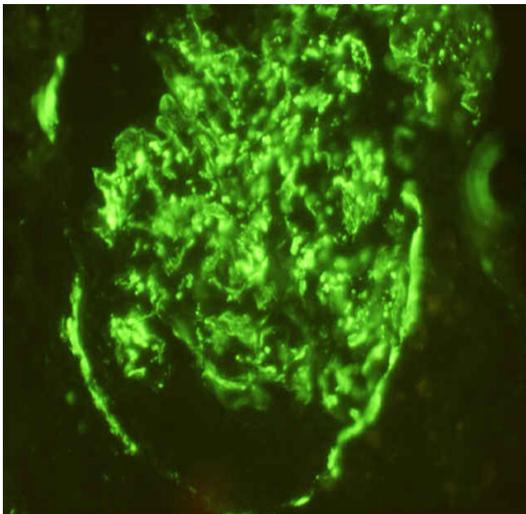


Figure 2. Immunofluorescence findings with intense mesangium deposits of C3.

serum creatinine was 116 $\mu\text{mol/l}$, and serum albumin was 2.8 g/dl. Serum anti-mycoplasma antibody titers was more than 1:160. Liver function parameters were within their normal limits. Urinalysis showed RBC > 200 per high power field (HPF), and urinary protein excretion was 900 mg/day. Antinuclear antibody, anti-DNA, anti-neutrophil cytoplasmic antibody, anti-glomerular basement membrane antibody, anti-HBs, and anti-HCV were all negative. Anti-streptolysin O was 488 U. Complement factors C3 was 0.17 g/l, C4 was within normal range. Serum levels of IgG, IgA and IgM were

normal. Renal biopsy was conducted, and in total 40 glomeruli were obtained and evaluated (**Figure 1**). 22 glomeruli had crescent formation (cellular crescents for 19 glomeruli, cell fibrous crescents for 3 glomeruli); meanwhile diffuse mesangial proliferation with increased cellularity and expanded matrix was observed in the majority of glomeruli. The widely compressed and occlusion of capillary lumen was noted. Segmental capillary loop necrosis was observed in 3 glomeruli. The widely vacuolar degeneration was observed in renal tubular epithelial cells. Renal interstitial area was infiltrated with mononuclear cells, neutrophils and plasma cells. Immunohistochemical staining showed exclusive mesangial deposition of C3 (**Figure 2**). Electro-microscope examination showed subepithelial deposition of electron dense material (**Figure 3**).

The patient received methylprednisolone pulse therapy (20 mg/kg/day for 3 continuous days), cyclophosphamide pulse therapy (750 mg/m²/month for 6 continuous months) and anti-infection treatment (cefmetazole, 100 mg/kg/day). Dipyridamole (4 mg/kg/day) and enalapril (10 mg/day) were also applied. Serum anti-mycoplasma antibody titers declined to less than 1:40 after the treatment for one month. Hematuria and proteinuria were decreased after double pulse therapy of methylprednisolone and cyclophosphamide. The urinary protein excretion declined to 200 mg/day after the

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treatment for 4 months. The serum levels of C3 and ASO returned to normal after 2, 6 months of the treatment, respectively. Urine RBC counts returned to normal after the treatment for 9 months.

Discussion

We reported a pediatric case with crescentic CPAGN with isolated C3 deposition. In this case, we applied the double pulse therapy of methylprednisolone and cyclophosphamide as well as anti-infection and -coagulation treatment. Favorable prognosis was achieved during the follow-up. Two previous reports [6, 7] also indicated successful treatment of two caucasians with CPAGN with isolated C3 deposition. Our study is the first report regarding Asian patient with CPAGN with isolated C3 deposition. Our findings suggested that patients with CPAGN with isolated C3 deposition may have a good prognosis with an effective treatment.

Several mechanisms may account for the influence of isolated C3 deposition on the prognosis of crescentic GN. First, complement is also an important aspect of defense against infection [8], the exclusive deposition of C3 at glomeruli was due to the disordered complement regulation. Isolated C3 deposition may occur with serious renal damage. CPAGN is a severe glomerular disease, which was associated with progressive worsening kidney function [9]. Meanwhile, the prognosis of CPAGN depends on the severity of the pathological features and the underlying disease [10]. In this sense, the isolated C3 deposition in CPAGN may affect the clinical presentation or prognosis of the disease. Second, dysregulated control of the alternative pathway of complement is an important risk factor for several renal diseases [11]. Complement activation also may account for the systemic inflammatory events that contribute to remote organ injury and patient mortality [12]. On the other hand, complement inhibitory drugs have now entered clinical use and may provide an important new therapeutic approach for patients with AKI [12]. Hence, it is reasonable to speculate that renal deposition of C3 may aggravate the clinical symptoms of various glomerular diseases.

In our report, however, we observed a favorable prognosis with only a relapse during the follow-

up, which might be due to the following facts: first, crescents were observed in half of the obtained glomeruli, the majority of the crescents were cellular crescents, which indicated the acute injury occurred in half of the glomeruli; the timely double pulse therapies of methylprednisolone and cyclophosphamide improved the glomerular injury. Second, in this case, the kidney function was not severely damaged, urinary protein excretion was mildly increased and the chest X-ray was normal. It is well-documented that the worsening kidney function, proteinuria and pulmonary infections will influence the therapeutic effects and prognosis. Therefore, the mild concomitant symptoms contributed to the favorable prognosis. Nevertheless, our findings still have important clinical implications that C3 deposition in the glomerulus may not significantly aggravate the severity of glomerular diseases; the timely aggressive immunosuppressive therapy may provide good effects.

In the past, a number of studies have also been performed to pay attention to C3GN. Medjeral-Thomas et al [13] reported that renal impairment at presentation predicted end-stage renal disease only among patients with dense deposit disease (DDD), not with C3GN. Zand et al [14] reported that patients with both C3GN and monoclonal gammaopathy treated with immunosuppressive agents showed significant decreases in hematuria and proteinuria and stabilization of kidney function. Sethi et al [15] reported that atypical post-infectious GN patients associated with abnormalities in the alternative pathway of complement did well with no significant decline in renal function in the short and long term after immunosuppressive treatment. Bridoux et al [16] reported that six adults with monoclonal gammaopathy and C3GN progressed to ESRD over a median period of 47 months. In terms of above-mentioned, C3GN might have a good response to various immunosuppressive agents; isolated C3 deposition might not affect the treatment effects.

Taken together, we reported successful treatment of CPAGN with isolated C3 deposition with aggressive immunosuppressive agents. Isolated C3 deposition in the glomerulus may not markedly aggravate the severity of CPAGN. However, further larger clinical studies should be performed to identify the influencing factors on the prognosis.

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Disclosure of conflict of interest

None.

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