

Case Report

Postinfectious Glomerulonephritis with Crescents in an Elderly Diabetic Patient after Acute Gastroenteritis: Case Report

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Keywords

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Abstract

Postinfectious glomerulonephritis (PIGN) is primarily a disease of childhood. It occurs after upper respiratory tract infection or skin infections. Streptococcus is the most common causative agent, but in the elderly, staphylococcus is the main culprit. In adults, PIGN is more common in immunocompromised patients, particularly diabetics and alcoholics. Here, we report the case of an elderly diabetic male who presented with severe acute kidney injury with active urinary sediment after acute gastroenteritis. Additional analyses revealed a very low serum C3 level and a normal serum C4 level. Renal biopsy showed diffuse proliferative glomerulonephritis with crescents. Direct immunofluorescence showed mesangial and capillary wall staining for C3 and IgG (2+, mesangial and segmental capillary wall, granular). Renal electron microscopy showed subepithelial hump-like electron-dense deposits. The role of steroid in the treatment of PIGN is controversial and there is no standard protocol, but our patient responded very well to steroid as he did not require hemodialysis after 2 weeks of initiation of steroid therapy. We should be aware of an atypical presentation of PIGN in elderly to ensure correct diagnosis.

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Introduction

Postinfectious glomerulonephritis (PIGN) is primarily a disease of childhood. It occurs after upper respiratory tract infection or skin infections [1, 2]. Streptococcus is the most common causative agent for PIGN in both children and adults [1–3]. Particularly in the elderly, staphylococcus is a common causative organism. Other pathogens include viral, fungal, protozoal and parasitic infection [4]. In adults, PIGN is more common in immunocompromised patients, particularly diabetics and alcoholics [4]. Crescent formation generally denotes severe glomerular injury. Morphologically, crescents are defined as extracapillary hypercellularity with two or more layers of cells in the Bowman space [5]. A direct relationship between the severity of renal disease and histological severity in this condition is not well established. Some studies showed a poor outcome in patients with crescents and some showed no such type of relationship [6, 7]. The role of steroids in the treatment of PIGN is debatable and there is no standard protocol. There is conflicting evidence supporting the use of steroids. Some studies showed good response, but in some studies, no correlation was found between the steroid use and outcome [6–9]. Here, we report a case of an elderly diabetic male who developed PIGN with crescents after acute gastroenteritis and responded very well to steroids.

Case Report

A 75-year-old male presented with a history of 1-week loose stools, nausea, vomiting, decreased urine output, and one episode of high-grade fever without any history of sore throat, skin infection, joint pain, respiratory tract infection, urinary tract infection, smoking, alcohol drinking, and NSAID abuse. There was a 10-year history of type 2 diabetes mellitus and a 2-year history of hypertension.

The patient's laboratory profile was as follows: hemoglobin: 11.1 g/dL, total leukocyte count: 12,700/mm³, platelet count: 2.8 × 10⁵/mm³, urinary protein: 3+, urinary sugar: 0, urine microscopy: white blood cell count: 30–40/high-power field, red blood cell count: 50–60/high-power field, urinary pH: –6, urinary albumin: 3+, urine culture: sterile, stool culture: *Escherichia coli*, serum albumin: 3.1 g/dL, serum sodium: 134.4 mEq/L, serum potassium: 4.1 mEq/L, serum calcium: 8.8 mg/dL, serum phosphorus: 5.2 mg/dL, random blood sugar: 182 mg/dL, blood urea: 103 mg/dL, serum creatinine: 7.3 mg/dL, serum anti-streptolysin O titer (ASO titer): <110 IU/mL, C3: 21.0 mg/dL (normal range: 90–180), C4: 17 mg/dL (normal range: 10–40), serum antinuclear antibody: negative, cytoplasmic antineutrophil cytoplasmic antibody: negative, perinuclear antineutrophil cytoplasmic antibody: negative, HBsAg: negative, anti-HCV: negative, HIV I and II: negative. Pharyngeal swab examination was negative. Ultrasonography abdomen showed bilateral normal size kidneys with increased bilateral renal cortical echogenicity and normal-size prostate. 2D echocardiography showed concentric left ventricular hypertrophy and left ventricular ejection fraction (58%). Fundus examination showed evidence of diabetic retinopathy. A renal biopsy showed diffuse endocapillary proliferative glomerulonephritis with cellular crescents over 2/13 (15.3%) glomeruli (Fig. 1). Tubular atrophy involved about 35% of sampled cortex. Tubules showed focally prominent cytoplasmic vacuolar change and evidence of patchy acute injury. Direct immunofluorescence showed mesangial and capillary wall staining for C3 (Fig. 2) and IgG (2+ mesangial and segmental capillary wall; granular) (Fig. 3). Renal electron microscopy showed thickened glomerular basement membranes, electron-dense deposits in mesangial, subepithelial and subendothelial regions of glomerular capillaries, subepithelial hump-like deposits and widespread

effacement of visceral epithelial cell foot processes (50–60%) (Fig. 4, 5). Thus, the diagnosis of PIGN with underlying diabetic nephropathy was made.

Treatment

We initiated treatment with intravenous antibiotics, diuretic (furosemide), antihypertensive drugs, and subcutaneous insulin for diabetes mellitus. Urine output did not improve in the first 24 h. Due to a high creatinine level and uremic symptoms, the next day hemodialysis was started. Urine analysis showed active sediments (red blood cells and white blood cells) and the serum C3 level was very low. Hemodialysis was continued on alternate-day basis as urine output did not improve. On the 10th day of admission, renal biopsy was done. It was suggestive of diffuse endocapillary proliferative glomerulonephritis with cellular crescents. Methyl prednisolone 500 mg was given once a day intravenously for 3 days and was followed by prednisone 1 mg/kg/day. After 14 days of steroid therapy, urine output was 1.2 L/day and serum creatinine was 3.8 mg/dL and hemodialysis was stopped. After 3 weeks of steroid therapy, the patient developed herpes zoster on the right side of the neck. The patient was treated with valacyclovir 1 g 3 times daily for 7 days. After 4 weeks of steroid therapy, creatinine was 1.9 mg/dL. ACE inhibitor was added in view of proteinuria (3.8 g/day). After 6 weeks of steroid therapy, the patient developed left leg cellulitis. He was treated with a combination of amoxicillin and clavulanic acid for 7 days. Steroid was tapered gradually over a period of 6 months. After 6 months, his creatinine level was 1.5 mg/dL and 24-h urine protein was 1.2 g/day.

Discussion

PIGN is an immune-mediated glomerulonephritis. Previously, most of the cases occurred in childhood and followed streptococcal upper respiratory tract or skin infections and were termed as poststreptococcal glomerulonephritis. In the past 3 decades, there is a major shift in epidemiology and outcome [10]. Because infection is usually ongoing at the time, glomerulonephritis is diagnosed, and the term infection-related glomerulonephritis has been suggested [11]. An immunocompromised background (diabetes or malignancy) is usually present for the development of PIGN in elderly [10]. Our patient was an elderly diabetic. The spectrum of causative pathogens, sites of infection, and duration of infection are different in the elderly as compared to children [10]. The sites of adult infection are more miscellaneous, including skin, upper respiratory tract, heart, lung, oral mucosa/teeth, and the urinary tract. However, our patient developed PIGN after acute gastroenteritis and stool culture showed *Escherichia coli*. Nasr et al. [6, 10] showed that *E. coli* can cause infection-related glomerulonephritis in adults. The time period between infection and onset of renal disease in children with PIGN is usually 1–6 weeks. But, in approximately half of elderly patients, the infection is first discovered at the onset of renal disease, indicating that infection may go unrecognized for some time [10]. Our patient had a history of one episode of high-grade fever with chills 1 week before and loose stools for 3 days 1 week before. The clinical differential diagnosis of PIGN in elderly is broad and includes other glomerular diseases associated with a low complement level, such as cryoglobulinemic glomerulonephritis, antineutrophil cytoplasmic antibody-associated pauci-immune glomerulonephritis, and C3 glomerulopathy [12]. The presence of a low level of C3 with normal C4 favors PIGN or C3 glomerulopathy, and low C4 with normal C3 is more typical of cryoglobulinemic glomerulonephritis [12]. However, up to one third of adults with PIGN have depression of both C3 and C4 [12]. In our patient, serum ASO titer, ANA,

cytoplasmic antineutrophil cytoplasmic antibody, and perinuclear antineutrophil cytoplasmic antibody were negative. He had a very low serum C3 level with a normal serum C4 level. After 2 months of disease onset, repeat serum C3 was normal.

On renal light microscopy, in PIGN the most common histological pattern of injury is diffuse endocapillary proliferative and exudative glomerulonephritis with numerous intracapillary neutrophils [12]. In our PIGN patient, renal light microscopy showed diffuse endocapillary proliferative glomerulonephritis with cellular crescents over 2/13 (15.3%) glomeruli (Fig. 1). Renal immunofluorescence in PIGN typically reveals C3-dominant or co-deposition of one or more immune reactants (IgG, IgM, IgA, C1q). IgG is usually the most frequent and intense immunoglobulin [12]. In our PIGN patient, renal immunofluorescence showed mesangial and capillary wall staining for C3 (Fig. 2) and IgG (2+ mesangial and segmental capillary wall; granular) (Fig. 3). In PIGN, renal electron microscopy by Nasr et al. [10] showed subepithelial electron-dense deposits in most cases (92% of patients), mesangial deposits (87% of patients), and small subendothelial deposits (66% of patients). In our PIGN patient, renal electron microscopy showed thickened glomerular basement membranes, electron-dense deposits in mesangial, subepithelial and subendothelial regions of glomerular capillaries, subepithelial hump-like deposits and widespread effacement of visceral epithelial cell foot processes (50–60%) (Fig. 4). Thickening of glomerular basement membrane was due to diabetic nephropathy and effacement of visceral epithelial cell foot processes were due to both diabetic nephropathy and PIGN.

There is no single pathognomonic clinical or pathologic finding for PIGN diagnosis in adults. At least three of the following criteria should be present [12]: (1) clinical or laboratory evidence of infection before or at the onset of glomerulonephritis, (2) decreased serum complement, (3) endocapillary proliferative and exudative glomerulonephritis, (4) C3-dominant or co-dominant glomerular immunofluorescence staining, and (5) hump-shaped subepithelial deposits on electron microscopy.

Our patient satisfied all 5 criteria for the diagnosis of PIGN. PIGN can be difficult to distinguish histologically from the C3 glomerulonephritis (C3GN) which is associated with abnormalities in the alternative pathway of complement. The glomerular positivity for C3 alone (i.e., without staining for IgG, IgM, IgA, or C1q) is an essential condition for C3GN, but can also occur in one fourth of patients who are in the resolving phase of PIGN [12]. The following features would favor C3GN over PIGN in patients with sole glomerular positivity for C3 [12]: lack of clinical evidence of infection, persistently low C3 for more than several months, persistently active glomerulonephritis for more than several months, and large mesangial, intramembranous and subendothelial deposits. The tendency of subepithelial deposits to localize into the mesangial “waist” and evidence of resorption within the subepithelial deposits on electron microscopy favor PIGN [12]. There is no clear-cut guideline to treat such a type of elderly patients with PIGN with crescents and the duration of therapy is not well defined. Crescentic glomerulonephritis having an underlying immune complex proliferative glomerulonephritis is less responsive to aggressive immunosuppressive therapy as compared to anti-glomerular basement membrane or antineutrophil cytoplasmic antibody crescentic glomerulonephritis but for the minority of patients who have idiopathic immune complex crescentic glomerulonephritis, the most common treatment is immunosuppressive therapy with pulse methylprednisolone, followed by prednisone at a dosage of 1 mg/kg daily tapered over the second to third month to an alternate-day regimen until completely discontinued [13]. Baikunje et al. [9] studied PIGN with crescents in adults and observed that those patients who were treated with steroids had excellent response, but the duration of therapy was variable. Our patient initially was on hemodialysis but after 2 weeks of steroid therapy hemodialysis

was stopped. Our patient responded very well to steroid therapy. To treat an elderly diabetic patient with immunosuppressive therapy is more challenging as our patient developed herpes zoster after 3 weeks of steroid therapy and left leg cellulitis after 6 weeks of steroid therapy.

Conclusion

PIGN should be kept in mind as a differential diagnosis among elderly patients with severe acute kidney injury and active urinary sediment. The associated organism may be non-streptococcal in elderly patients having PIGN with crescents. Greater understanding of the atypical presentation of PIGN in elderly patients is needed to ensure correct diagnosis.

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Statement of Ethics

The authors followed the guidelines for human studies and the research was conducted ethically. Information revealing the subject's identity was avoided. Guardians have given their written informed consent to publish this case, including publication of images.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Satyanand Sathi and Anil Kumar Garg contributed to manuscript design, data interpretation, manuscript review and drafting of the manuscript. Ajay Kumar Singh contributed to manuscript review. Manoj Kumar Singh and Virendra Singh Saini contributed to final drafting and critical revision of the manuscript. All the authors approved the final version of the manuscript.

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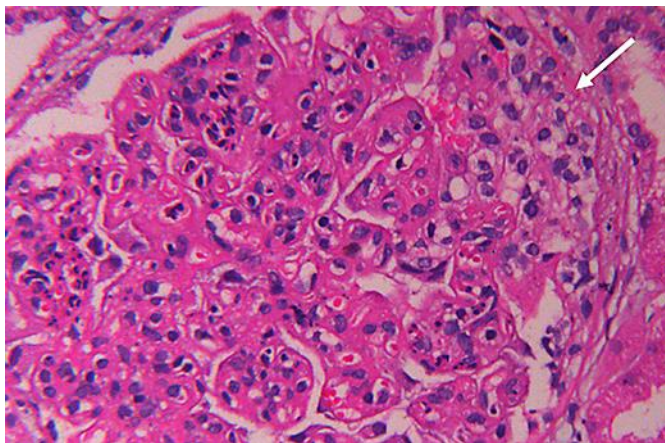


Fig. 1. Kidney biopsy specimen shows endocapillary proliferative glomerulonephritis with a cellular crescent at the 1 o'clock to 3 o'clock position in the tuft (arrow).

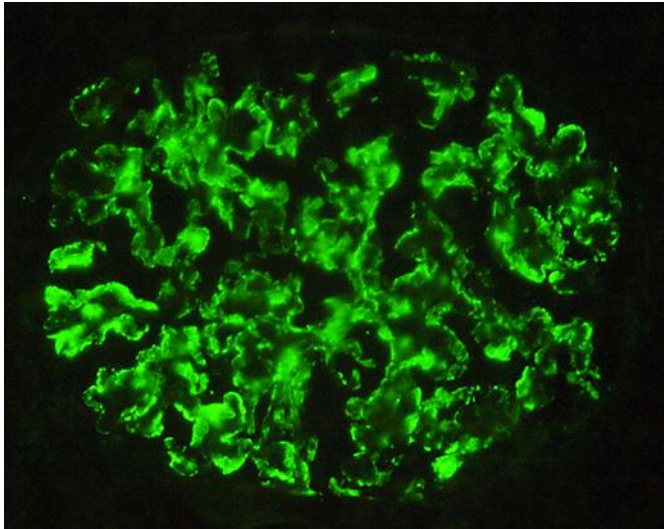


Fig. 2. Kidney biopsy specimen shows mesangial and capillary wall staining for C3.

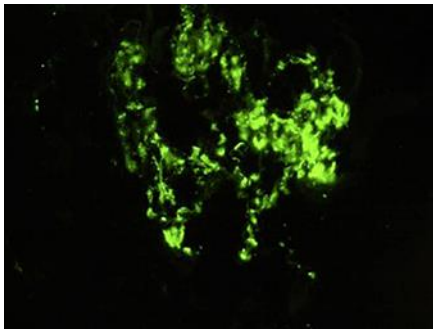


Fig. 3. Kidney biopsy specimen shows IgG (2+ mesangial and segmental capillary wall; granular).



Fig. 4. Kidney biopsy specimen on electron microscopy shows large subepithelial (hump-like) electron dense deposits (arrows).

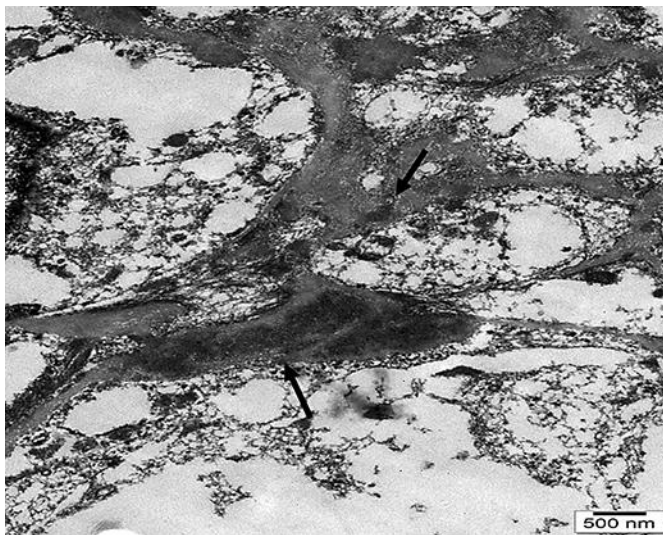


Fig. 5. Kidney biopsy specimen on electron microscopy shows scattered mesangial and subendothelial electron dense deposits (arrows).