Post-Infectious Glomerulonephritis in Elderly Patients

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Abstract

Post-Infectious Glomerulonephritis (PIGN) is a disease of childhood. It is an important cause of acute kidney injury in childhood. It is now frequently identified in elderly people with compromised immune status and risk factors like malignancy and diabetes mellitus (DM).

We have reported two cases of patients (age: 61 years and 80 years) which presented to us with unexplained renal failure. Both patients required renal replacement therapy (RRT) in the form of hemodialysis for their renal failure. Auto-immune workup for both patients was negative. Renal biopsy was performed and a diagnosis of PIGN was established on the basis of histopathological characteristics. We treated both cases with intravenous antibiotics. Renal parameters of both patients started improving and both achieved full renal recovery on long-term follow-up of 18 months.

PIGN can be seen in the adult population and should not be considered solely a childhood disease.

Keywords: *Post-infectious Glomerulonephritis (PIGN), streptococcus, staphylococcus, rapidly progressing renal failure (RPGN).*

INTRODUCTION

PIGN is primarily known for causing rapidly progressing glomerulonephrtis (RPGN) in childhood. Streptococcus infection following pharyngitis or impetigo is considered the classic etiologic factor for PIGN. An epidemiologic change in PIGN demographics has been observed with the global decline in disease in childhood population particularly in developed countries and it is now coming into seen in older populations particularly with comorbidity like diabetes [1]. Around 1/3rd of adults with PIGN are found to have at least one comorbid factor. In adults, PIGN is frequently seen with staphylococcus infection. The exact pathogenesis is not clear. A different pathogenic mechanism of nephritis may be responsible that may include a super antigen (exotoxin toxic shock syndrome toxin) related to staphylococcus infection which stimulates high cytokine activity and IgA immune-complex deposition in the glomerular basement membrane [2].

Here we are reporting two cases of PIGN in adults having a history of hepatitis C infection and achieved complete renal recovery in both cases.

CASE REPORT

CASE I: A 61-year-old diabetic, hypertensive, hepatitis C positive female presented with generalized body swelling, shortness of breath and decreased urine output. The patient had no history of fever, cough, sputum, palpitation, epistaxis, hemoptysis, rash or joint pains. She was treated for hepatitis C 3 years back with interferon and ribavirin for 6 months. Her drug history included Metformin, Gliclazide, Lisinopril, Furosemide and Spironolactone. On presentation, she had BP of 140/90 mmHg, Pulse of 90 b/min, Respiratory rate of 30 breaths/min and was afebrile. She had pitting edema of 3+. On systemic examination, she had crackles till mid zone in bilateral lung fields, while the rest of systemic examination was unremarkable. Lab workup showed slightly low hemoglobin of 10 g/dl, TLC 11x10^9 /L and platelet 175000/ microliter of blood. Her Urea was 89 mg/dl, creatinine 2.5 mg/dl, Na 132 mEq/L, K 4.0 mmol/L, Hco3 22 mEq/L, Cl 99 m.mol/L, Calcium 8.4 mg/dl. The liver function test was normal, Albumin was low at 2.4gm/dl. Urine detailed report showed Proteins of 150mg, RBC 14-18 cells/ microliter, Glucose 3 mmol/l, Pus cells 10-12 cells/ microliter. Urine was positive for dysmorphic cells. Spot urine protein to creatinine ratio was raised at 10 (**Table 1a**). Ultrasound was done which showed normal-sized kidneys with a right kidney of 10.1*1.2 cm and a left kidney of 10.5*1.1 cm. During the hospital stay, the patient was treated with intravenous

Table 1a: Laboratory data.

Parameter	Results
Hemoglobin	10 g/dl
Total Leukocyte count TLC	11x 109 /L
Platelet	175000/ microliter of blood
Urea	89 mg/dl
Creatinine on admission	2.5 mg/dl
Creatinine on OPD follow up	0.8 mg/dl
Sodium Na	132 mEq/L
Potassium K	4.0 mmol/L
Chloride	99 m.mol/L
Calcium	8.4 mg/dl
Serum HCO3	22 mEq/L
C3	80 mg/dl (88-252mg/dl)
C4	10 mg/dl (12-75mg/dl).
ANA	All Negative
Albumin	2.4gm/dl.
Spot urine Protein and creatinine ratio	10

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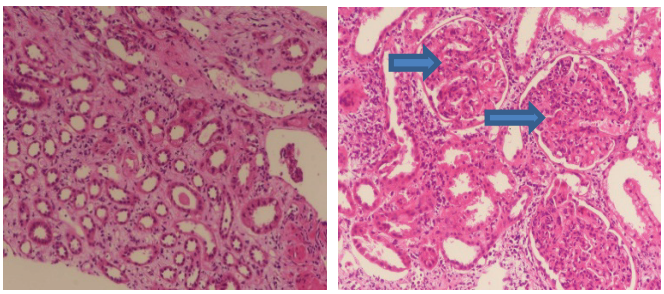
Table 1b: Biopsy findings.

Technique	Results
Light Microscopy	● Total 6 glomeruli exhibiting endocapillary proliferation. ● Neutrophils were seen within the capillaries ● No definite neutrophil in mesangium. ● No sclerosis ● Interstitium showed mild to moderate inflammation.
Immunoflorescence	● IgM +ve ● C1q +++ve (membrane plus mesangium) ● C3c +++ve (membrane plus mesangium) ● IgG Negative ● IgA Negative



Light microscopic picture with H&E staining
Fig. (1): Interstitium showing intact tubules with mild to moderate inflammation.
Fig. (2): Glomeruli with closed capillary loops suggesting endocapillary proliferation <arrow head>.

antibiotics and had multiple sessions of hemodialysis and ultrafiltration. Her autoimmune workup showed ANA negative and low C3 at 80 mg/dl (88-252mg/dl) and low C4 at 10 mg/dl (12-75mg/dl). Considering unexplained renal failure her renal biopsy was done. The biopsy report showed a total of 6 glomeruli exhibiting endocapillary proliferation. Neutrophils were seen within the capillaries with no definite neutrophil in the mesangium. There were no spikes, membrane thickening, double contouring or any signs of sclerosis. The interstitium showed mild to moderate inflammation. Immunofluorescence revealed IgM +ve, C1q and C3c +++ve (membrane plus mesangium), while IgG and IgA were negative (**Table 1b**) (**Figs. 1&2**). Final diagnosis of Proliferative glomerulonephritis most likely post-infectious glomerulonephritis was established. The patient's renal parameters gradually started improving within a week and she started making good urine output. The patient was followed in the clinic and long-term follow-up up to 18 months showed complete renal recovery with a creatinine of 0.8 mg/dl.

CASE II: A 80-year-old hypertensive and hepatitis C positive female presented with generalized body swelling, abdominal distension and shortness of breath. The patient had no history of flu, rash, joint pains or bleeding. The patient was referred from a periphery hospital where she was admitted for a week and was managed for acute renal failure with volume overload. She has sessions of hemodialysis with ultrafiltration. The patient had a history of cholecystectomy and an untreated hepatitis c infection. The patient had a drug

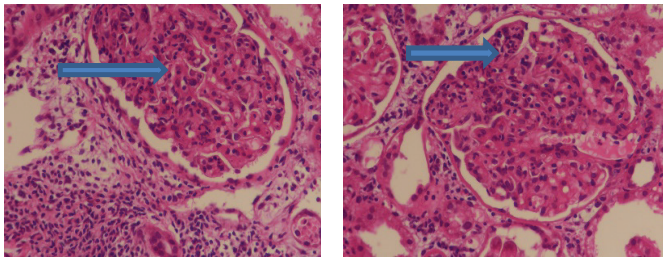
Table 2a: Laboratory data.

Parameter	Results
Hemoglobin	9.6 g/dl
Total Leukocyte count TLC	6.5 x 109 /L
Platelet	294000/ microliter of blood
Urea	193 mg/dl
Creatinine on admission	3.4 mg/dl
Creatinine on OPD follow up	1.0 mg/dl
Sodium Na	134 mEq/L
Potassium K	6.1 mmol/L
Chloride	98 m.mol/L
Calcium	8.2 mg/dl
Serum HCO3	22 mEq/L
C3	100 mg/dl (88-252mg/dl)
C4	24 mg/dl (12-75mg/dl).
ANA	All Negative
Albumin	2.0 gm/dl.
24 Hour urine Protein and creatinine	1470mg/l.

Table 2b: Biopsy findings.

Technique	Results
Light Microscopy	● Total 14 glomeruli ● 3 glom diffuse mesangiocapillary proliferation. ● Neutrophils were seen within the capillaries ● 7 glomeruli showed collapsed and wrinkled ● capillary walls with tortuous membranes. ● 4 globally sclerosed ● Interstitium showed moderate acute and chronic inflammation. ● Small arteries showed mild fibrointimal thickening.
Immunoflorescence	● IgM Equivocal ● C1q ++ve (membranous and mesangial, granular) ● C3c ++ve (membranous, granular) ● IgG ++ve (membranous, granular)

history of carvedilol and hydralazine. The patient was vitally stable with a BP of 120/70 mmHg, Pulse 88 b/min, Respiratory rate of 28 breaths/min and she was afebrile. On systemic examination patient had bilateral basal crackles in both lung fields, the abdomen was soft, distended with positive fluid thrill and shifting dullness, all other systemic examination was unremarkable. Her lab workup showed a low Hb of 9.6 g/dl, with normal TLC 6.5 x 109 /L and Platelet 294000/ microliter of blood. Her Urea was 193 mg/dl, creatinine of 3.4 mg/dl, potassium 6.1 mEq/L, Na 134 mEq/L, HCO3 22 mEq/L, Cl 98 mmol/L, Ca 8.2 mg/dl, PO4 5.8 mg/dl, Mg 2.5 mg/dl, albumin of 2.0 g/dl. Her liver function test was normal. Her urine detailed report showed Protein of 250mg, RBC Numerous, Pus cells of 2-3 cells/microliter. Her 24-hour urine protein was 1470mg/l (**Table 2a**). On ultrasound of kidneys, the right kidney was 9.4*1.0cm and left kidney 9.4*1.2 cm. Multiple sessions of hemodialysis and ultrafiltration were done. Autoimmune workup showed ANA negative with normal C3 and C4 of 100 mg/dl and 24 mg/dl respectively. Provided unexplained nature of her renal failure renal biopsy was done that showed a total of 14 glomeruli; 4 glomeruli were globally sclerosed, 3 glomeruli showed diffuse mesangiocapillary proliferation along with neutrophilic infiltration, 7



Light microscopic picture with H&E staining
Figs. (3&4): Glomeruli showing closed capillary loops and busy mesangium suggestiveof diffuse mesangiocapillary proliferation <arrow head> Interstitium showing increased inflammatory cells.

glomeruli showed collapsed and wrinkled capillary walls with tortuous membranes. Tubules were unremarkable. The interstitium showed moderate acute and chronic inflammatory cell infiltrates comprising lymphocytes, plasma cells, neutrophils and eosinophils. Small arteries showed mild fibrointimal thickening. Immunofluorescence showed IgM Equivocal, IgG and C3c ++ve (membranous, granular) and C1q ++ve (membranous and mesangial, granular) (**Table 2b**) (**Figs. 3&4**). The patient was diagnosed with diffuse proliferative glomerulonephritis most likely post-infectious glomerulonephritis. Her renal parameters gradually started improving. She achieved Long term complete renal recovery on long-term follow-up of 18 months with serum Cr of 1.0 mg/dl.

DISCUSSION

Infectious etiologies are very well described as a cause of acute kidney injury since the mid of 800s. Acute post-infectious glomerulonephritis (PIGN) is an immunological process following an infection caused by Streptococcus and results in acute kidney failure. The disease was previously considered a typical childhood disease developing after throat or skin infection secondary to beta-hemolytic Streptococcus. Immune-complex-related pathogenesis exists in which Molecular mimicry between soluble streptococcal antigens (*e.g.* SpeB and FimH) cross-react with glomerular proteins including laminin, vimentin and collagen. This cross-reaction results in antibody-mediated damage to the glomerular basal membrane [3]. PIGN has now almost disappeared from the developed world but the classic childhood form is still present in the developing part of the world. The estimated incidence in developing countries is more than 200 cases per million population (pmp)/year [4] and according to an observation the incidence is estimated even greater than this due to unregistered cases of epidemic clustering of PIGN in developing countries [5].

However, there is noted a transition of disease from pediatrics to the adult population in the developed countries. The disease in the adult population came into notice for the 1st time in Italy when an epidemiological evaluation showed an incidence of PIGN more than double in the elderly than in the pediatric population [6]. We have reported two cases of PIGN in the elderly with comorbidity like diabetes mellitus (DM). Predisposing factors for PIGN in adults are diabetes, malignancy, intravenous (iv) drug-abuser and severe vasculopathy [7].

Various differences of PIGN in adults are identified from classic pediatric PIGN. In contrast to classic PIGN for which beta-hemolytic Streptococcus is the main etiological bacteria, adult PIGN usually follows infection with Staphylococcus aureus (both methicillin-susceptible (MSSA) & methicillin-resistant (MRSA) [8]. The classic PIGN commonly follows skin and throat infection while adult PIGN may follow remote site infection including Urinary tract infection (UTI), skin infection, viral or even fungal infections. It typically presents as a nephritic syndrome with hematuria (macro- or microscopic), raised blood pressure (hypertension), proteinuria, edema and renal failure of variable severity. In a study of 2011, 109 cases in the elderly with PIGN were identified in which different offending bacteria are found from the typical childhood disease including staphylococci (24 to 60%) including S. epidermidis and S. aureus, streptococci (16 to 30%), gram-negative cocci including E-coli, acinatobactor and pseudomonas, Chlamydia, Mycoplasma, fungi like Candida, Histoplasma, viruses like HSV, CMV, EBV, HBV, influenza, RSV and parasites including Toxoplasma and Plasmodium malaria [9].

Renal biopsy is usually not required for childhood disease and is characterized by proliferative glomerulonephritis (GN) with diffuse hypercellularity. The cellular infiltration is exudative and consisting neutrophils, monocytes, rare lymphocytes with CD68, CD3, CD20 and endothelial cells. Capillary lumen and urinary space are reduced. In contrast, in old patients, renal biopsy is indicated in case of rapidly progressive renal failure, non-resolving or delayed resolving renal failure, nephrotic range proteinuria and persistently low C3. Histology is characterized by IgA-dominant deposits. Rarely, crescents and severe interstitial inflammation are seen. Despite all differences in PIGN of two age groups the therapy mainly remains the same and consists of culture-guided systemic antibiotics. A small change is the use of steroids in selected cases of adult PIGN say for example; biopsy positive for crescents.

The prognosis for the elderly population is defined to be poor with 33% progressing to end-stage renal disease <ESRD> and full renal function recovery in fewer than 25% cases [10]. In another review article, 60% progression to ESRD is mentioned [11], in our case both patients were required renal replacement therapy (RRT) in the form of hemodialysis but they achieved full renal recovery on long-term follow-up.

Authors suggest considering PIGN as an important possible cause of unexplained renal failure in elderly patients.

CONCLUSION

PIGN as showing a transition from pediatrics population to adult in the developed worlds is the disease of adult in our part of the world as well. It should be considered as a possible cause of renal failure in elderly patients with otherwise unexplained rapidly progressing renal failure.

CONSENT FOR PUBLICATION

Consent for publication taken from both patients after explaining academic reason for publication and maintenance of confidentiality by not mentioning personal information of patients in final publication.

CONFLICT OF INTEREST

Authors declare no conflicts of interest.

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Declared none.

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