J Ped Nephrol
Journal of Pediatric Nephrology
Spring 2023. Volume 11. Number 2

Case Report

IgA-dominant Infection-related Glomerulonephritis in a 13-year-old Child: A Case Report and Brief Review of Literature

Ipshita Magh[1], Lipsa Priyadarshini[1], Subal Kumar Pradhan[1*]

1. Division of Pediatric Nephrology, Department of Pediatrics, SVPPGIP and Srirama Chandra Bhanja Medical College and Hospital, Cuttack, India.

Use your device to scan and read the article online

Citation Magh I, Priyadarshini L, Pradhan SK. IgA-dominant Infection-related Glomerulonephritis in a 13-year-old Child: A Case Report and Brief Review of Literature. Journal of Pediatric Nephrology. 2023; 11(2):109-113. https://doi.org/10.22037/jpn.v12i2.43027

https://doi.org/10.22037/jpn.v12i2.43027

Article info:
Received: 19 Aug 2022
Accepted: 29 Jan 2023
Publish: 01 Apr 2023

Corresponding Author:
Subal Kumar Pradhan
Address: Division of Pediatric Nephrology, Department of Pediatrics, SVPPGIP and Srirama Chandra Bhanja Medical College and Hospital, Cuttack, India.
E-mail: drsubal@rediffmail.com

ABSTRACT

There has been a history of various bacterial infections and glomerular injuries, which are now pooled under the terminology of infection-related glomerulonephritis (IRGN). IRGN is an immune complex-mediated glomerulonephritis (GN) preceded by infection with subsequent recovery of renal function after the resolution of the infection. Pediatric IgA-dominant infection associated with GN is rare and generally has a favorable prognosis compared to adults with severe comorbidities, like diabetic nephropathy. We reported a 13-year-old girl presented with acute kidney injury with nephritic features with no history of concurrent illness.

Keywords: IgA, Glomerulonephritis, IgA nephropathy, Child

Introduction

Infection-related glomerulonephritis (IRGN) is an umbrella term including entities, such as post-infectious glomerulonephritis (PIGN), IgA-dominant IRGN, endocarditis-related GN, and shunt nephritis. It typically occurs after 1-2 weeks of upper respiratory tract infection and 1-4 weeks after cutaneous infection [1, 2].

Most cases of non-streptococcal IRGN occur concurrently and at times before the diagnosis of infection. Therefore, the proposed term IRGN more accurately describes this pathology than the old PIGN term [3].

The mechanism involving IgA-dominant IRGN was found to be immune-mediated leading to immune complex formation and renal injury typically caused by but not limited to *Staphylococcal aureus* infection. It has been documented to have diverse presentations, includ-

J Ped Nephrol
Journal of Pediatric Nephrology

ing etiology and immunofluorescence studies, and has been less widely studied, mostly in a pediatric population [3, 4] The most common presentation is acute nephritic syndrome, including proteinuria, hematuria, edema, hypertension, and reduced renal function. Typically, PIGN with its self-limiting nature has a better prognosis in children, i.e. it is treated without progression, as opposed to adults, which leads to chronic kidney disease (CKD) and end-stage renal disease (ESRD). A very close distinction is C3 glomerulopathy, which is caused by host genetic abnormalities that lead to dysregulation of the complement pathway and lead to nonresolving CKD. Hence, it becomes immensely important to differentiate the two entities for early recognition and intervention.

We reported a 13-year-old girl presented with acute nephritic syndrome with acute kidney injury (AKI) with renal biopsy suggestive of IgA-dominant infection-related glomerulonephritis with progressive renal dysfunction.

Case Presentation

A 13-year-old girl was referred to the hospital with chief complaints of swelling of both eyelids followed by abdomen and bilateral legs for seven days with decreased urination for two days. There was a history of febrile upper respiratory tract infection a week ago. Her birth history and developmental history were uneventful. she had received all her vaccinations as per the national immunization schedule.

On admission, she was conscious, well-oriented, and normothermic; the respiratory rate was 20/min, pulse rate was 120/min with regular rhythm, and blood pressure was 130/90 mmHg (95^{th}-95^{th} +12 mmHg). On clinical examination, she had periorbital puffiness and bilateral pitting pedal edema; anthropometry revealed her weight of 37.3 kg (10^{th}-25^{th} percentile, IAP chart) and height of 144.2 cm (10^{th}-25^{th} percentile, IAP chart). Systemic examination was normal except for mild ascites.

Her initial lab reports were suggestive of anemia (Hb: 8.7 gm/dL) and deranged renal function and the following results were obtained: -blood urea: 193.9 mg/dL (15-40 mg/dL), serum creatinine: 7.93 (0.7-1.5 mg/dL), quantitative C-reactive protein (CRP-Q): 17.7 (0-6 mg/dL), urine albumin: 3+, spot urine protein/urine creatinine ratio: >2 (normal <0.2), and aspartate aminotransferase (AST): 16.8 IU/L (12-40), alanine transaminase (ALT): 7.8 IU/L (8-40), alkaline phosphatase (ALP): 92 IU/L (<360) indicating normal liver function. On further evaluation, the sickling test was negative, serum C3 levels were 1.77 g/L (0.90-1.80 g/L), and anti-streptolysin O (ASO) titer and antinuclear antibodies (ANA) were negative. Blood culture reported no growth. Two-dimensional echocardiography revealed normal biventricular function. Abdominal ultrasound revealed bilateral echogenic kidneys of normal size (right kidney: 10.3×4.5 cm and left kidney: 10.3×4.6 cm). However, she had persistent oliguria for more than two weeks. Therefore, renal biopsy was done where light microscopy revealed diffuse proliferative glomerulonephritis with intracapillary and mesangial mononuclear cell/neutrophil infiltration with crescents (Figure 1). A crescent was observed in more than 61% of glomeruli. Immunofluorescence study revealed extensive glomerular immune complex deposits of IgA (3+), IgG (2+), C3 (2+), IgM (1+), and Kappa light chains (2+) suggestive of IgA-dominant IRGN with rapidly progressive glomerulonephritis.

Due to persistent oliguria and progressive azotemia, hemodialysis was started. Blood pressure was controlled with an amlodipine tablet (0.3 mg/kg/day)

She was treated with three doses of pulse methylprednisolone, followed by oral prednisolone and hemodialysis support. As she did not respond to steroids and had persistent oliguria with hypertension, cyclophosphamide (tablet, 2 mg/kg/day) was given. Due to persistent AKI and the need for repeated hemodialysis, the permanent central venous catheter was inserted in the right internal jugular vein. She gradually improved and was discharged with follow-up recommendations, including intermittent hemodialysis and catheter care at the local hospital. Prior to discharge, her deranged renal function was in the declining trend with blood urea of 88 mg/dL and serum creatinine of 1.8 g/dL.

At subsequent follow-up four months later, initial investigations revealed hemoglobin levels of 7.2 g/dL and deranged RFT (urea=117.1 mg/dL and creatinine=3.69 mg/dL) with normal electrolytes and liver function test and she underwent two cycles of hemodialysis. Serum vitamin D (17.10 ng/mL) and phosphorous (1.92 mg/dL) levels were low and abdominal ultrasound showed the right kidney of 9.2×4.2 cm and left kidney of 9.1×4.0 cm with gross ascites. She was diagnosed with CKD and her parents were counseled about the course of the disease with available renal replacement therapy options. She was discharged with supplements and follow-up recommendations, including regular hemodialysis twice weekly and catheter care at a local hospital.

Discussion

In a classic case of PIGN, the immune complex deposition was found to be predominantly of IgG type and mainly in the subepithelial region of the glomerular BM caused by nephritogenic strains of group A streptococcus. It is usually self-limiting and has an excellent prognosis in children. IgA-dominant IRGN is another form of GN, which develops during an ongoing infection typically due to *S. aureus*, which has not been extensively studied. It was first investigated by Nasr et al. in 2003 in adults and they showed poor results with no patient achieving complete recovery to baseline creatinine [3]; four of the study population progressed to renal failure and one patient achieved partial improvement [4, 5].

In PIGN, the clinical presentation can vary from asymptomatic hematuria and proteinuria to nephritic syndrome. Renal function with elevated serum creatinine and serologic studies with ASO or anti-DNAse B antibodies are usually positive, indicating recent streptococcal infection. Low complement levels with typically low C3 and normal C4 levels are a universal feature during the active disease phase. This disease is usually self-limiting with improving complement levels [6, 7].

IgA-dominant IRGN is set with AKI in the background of a persistent infection, usually due to *S. aureus*; hypocomplementemia is reported in 60% of cases, of whom 20-80% have persistent renal dysfunction progressing to end-stage renal disease and hence, requires early and prompt diagnosis to preserve kidney function [1, 8-11]. IgA nephropathy in its early course and during its recovery or persistent lesions is identical to IgA-dominant IRGN, which needs to be distinguished for better and early treatment [6, 12]. Serum complement levels are normal in IgA nephropathy, whereas hypocomplementemia occurs in about 35-100 % of IRGN cases [6, 7].

Clinically, the course and prognosis of classical IgA nephropathy are quite different, where IRGN has a better prognosis and IgA nephropathy if untreated, can progress to RPGN. Differential biopsy findings of IRGN, IgA-dominant IRGN, and IgA nephropathy are shown in Table 1. The main treatment for IRGN is to fight the infection with appropriate antibiotics and symptomatic therapy. No significant finding was found in studies on the use of steroids and cyclophosphamide for IRGN treatment [13-17].

In our patient, after a complete workup, the source of the infection could not be identified, her lab reports suggested decreased renal function with oliguria, and she underwent several cycles of hemodialysis. Simultaneously, a renal biopsy was taken to assess the extent of renal dysfunction, which revealed features suggestive of IgA-dominant IRGN with RPGN and low serum complement levels (both C3 & C4).

This required us to act judiciously to preserve her renal function; however, due to the lack of studies in the pediatric population at present, this posed a significant challenge to our treatment protocol. Therefore, more emphasis is placed on the need for kidney biopsy in the diagnosis of various IRGN entities for rapid diagnosis and early intervention.

Table 1. Differential biopsy findings of IRGN, IgA-Dominant IRGN, and IgA nephropathy

Pathology	IRGN	IgA-dominant IRGN	IgA Nephropathy (IgAN)
Light microscopy	Prominent endocapillary hypercellularity with neutrophilic infiltration. Acute exudative GN.	Endocapillary hypercellularity, the same picture as IRGN.	Uncommon acute exudative GN pattern and heterogeneity findings, predominantly show mesangial hypercellularity with increased mesangial matrix.
Immunofluorescence study	C3 complement staining with/ without Ig (IgG). Long capillary walls: "Garland" pattern, active phase. Randomly scattered fine and coarse granular staining within mesangium and capillary walls: "Starry-sky" pattern. Granular staining primarily in mesangial areas: "Mesangial" pattern. Lambda chain: +/-.	IgA deposition. Kappa chain dominance.	Granular IgA deposits localized to mesangium. C3 complement commonly co-deposited. The presence of C1q deposition reveals the possibility of secondary IgAN. Lambda chain dominance.
Electron microscopy	Subepithelial hump-shaped deposits.	Numerous subepithelial hump deposits with IgA.	Predominantly deposits presented in the glomerular mesangium.

J Ped Nephrol
Journal of Pediatric Nephrology

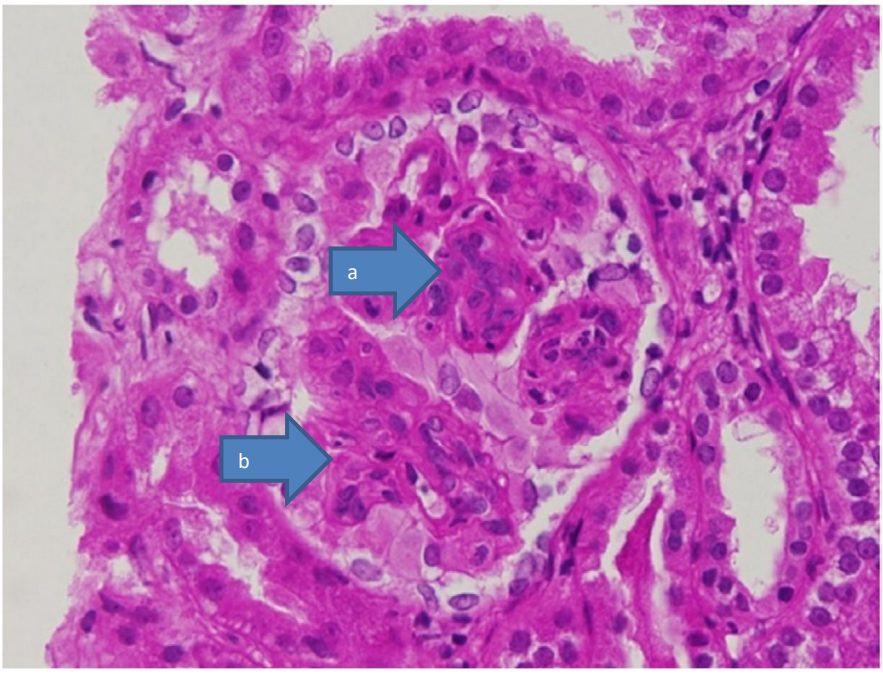

Figure 1. Light microscopy using Hematoxylin & Eosin (H&E) staining indicating mesangial proliferation (a) and neutrophilic infiltration (b)

Conclusion

IRGN is an immune-complex mediated process predominantly due to IgA deposition in response to an ongoing infection, mostly caused by *S. aureus*. Its incidence in the pediatric population is rare as it is understudied. The prognosis and courses might be different from IgA nephropathy; IRGN can rapidly progress to RPGN if left untreated and therefore, prompt diagnosis and treatment are important to prevent further damage as it has a good prognosis in children compared to adults.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research. The consent was obtained.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors

Authors' contributions

Conceptualization, writing, review and editing: Subal Kumar Pradhan and Lipsa Priyadarshini; Software, investigation, resources and writing the original draft: Ipshita Magh; Methodology, formal analysis, visualization, supervision and project administration: Subal Kumar Pradhan; Data curation: Lipsa Priyadarshini; Validation: All authors.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Nasr SH, D'Agati VD. IgA-dominant postinfectious glomerulonephritis: A new twist on an old disease. Nephron Clin Pract. 2011; 119(1):c18-25; discussion c26. [PMID]

[2] Glassock RJ, Alvarado A, Prosek J, Hebert C, Parikh S, Satoskar A, et al. Staphylococcus-related glomerulonephritis and poststreptococcal glomerulonephritis: Why defining "post" is important in understanding and treating infection-related glomerulonephritis. Am J Kidney Dis. 2015; 65(6):826-32. [DOI:10.1053/j.ajkd.2015.01.023] [PMID]

[3] Nasr SH, Fidler ME, Valeri AM, Cornell LD, Sethi S, Zoller A, et al. Postinfectious glomerulonephritis in the elderly. J Am Soc Nephrol. 2011; 22(1):187-95. [DOI:10.1681/ASN.2010060611] [PMID]

[4] Nasr SH, Markowitz GS, Whelan JD, Albanese JJ, Rosen RM, Fein DA, et al. IgA-dominant acute poststaphylococcal glomerulonephritis complicating diabetic nephropathy. Hum Pathol. 2003; 34(12):1235-41. [DOI:10.1016/S0046-8177(03)00424-6] [PMID]

[5] Handa T, Kakita H, Tateishi Y, Endo T, Suzuki H, Katayama T, et al. The features in IgA-dominant infection-related glomerulonephritis distinct from IgA nephropathy: A single-center study. Clin Exp Nephrol. 2018; 22(5):1116-27. [DOI:10.1007/s10157-018-1564-4] [PMID]

[6] Hunt EAK, Somers MJG. Infection-related glomerulonephritis. Pediatr Clin North Am. 2019; 66(1):59-72. [DOI:10.1016/j.pcl.2018.08.005] [PMID]

[7] Satoskar AA, Nadasdy G, Plaza JA, Sedmak D, Shidham G, Hebert L, et al. Staphylococcus infection-associated glomerulonephritis mimicking IgA nephropathy. Clin J Am Soc Nephrol. 2006; 1(6):1179-86. [DOI:10.2215/CJN.01030306] [PMID]

[8] Worawichawong S, Girard L, TrpkovK,Gough JC, Gregson DB, Benediktsson H. Immunoglobulin a-dominant postinfectious glomerulonephritis: Frequent occurrence in nondiabetic patients with Staphylococcus au-reus infection. Hum Pathol. 2011; 42(2):279-84. [DOI:10.1016/j.humpath.2010.07.009] [PMID]

[9] Khalighi MA, Al-Rabadi L, Chalasani M, Smith M, Kakani S, Revelo MP, et al. Staphylococcal Infection-related glomerulonephritis with cryoglobulinemic features. Kidney Int Rep. 2018; 3(5):1128-34. [DOI:10.1016/j.ekir.2018.05.010] [PMID]

[10] Nasr SH, Markowitz GS, Stokes MB, Said SM, Valeri AM, D'Agati VD. Acute postinfectious glomerulonephritis in the modern era: Experience with 86 adults and review of the literature. Medicine. 2008; 87(1):21-32. [DOI:10.1097/md.0b013e318161b0fc] [PMID]

[11] Kambham N. Postinfectious glomerulonephritis. Adv Anat Pathol. 2012; 19(5):338-47. [DOI:10.1097/PAP.0b013e31826663d9] [PMID]

[12] Haas M, Racusen LC, Bagnasco SM. IgA-dominant postinfectious glomerulonephritis: A report of 13 cases with common ultrastructural features. Hum Pathol. 2008; 39(9):1309-16.[DOI:10.1016/j.humpath.2008.02.015] [PMID]

[13] Khalighi MA, Wang S, Henriksen KJ, Bock M, Keswani M, Meehan SM, et al. Revisiting post-infectious glomerulonephritis in the emerging era of C3 glomerulopathy. Clin Kidney J. 2016; 9(3):397-402. [DOI:10.1093/ckj/sfw032] [PMID]

[14] Bu R, Li Q, Duan ZY, Wu J, Chen P, Chen XM, et al. Clinicopathologic features of IgA-dominant infection-associated glomerulonephritis: A pooled analysis of 78 cases. Am J Nephrol. 2015; 41(2):98-106. [DOI:10.1159/000377684] [PMID]

[15] Arivazhagan S, Lamech TM, Myvizhiselvi M, Arumugam V, Alavudeen SS, Dakshinamoorthy S, et al. Efficacy of corticosteroids in infection-related glomerulonephritis-a randomized controlled trial. Kidney Int Rep. 2022; 7(10):2160-5. [DOI:10.1016/j.ekir.2022.07.163] [PMID] [PMCID]

[16] Sethi S, Fervenza FC, Zhang Y, Zand L, Meyer NC, Borsa N, et al. Atypical postinfectious glomerulonephritis is associated with abnormalities in the alternative pathway of complement. Kidney Int. 2013; 83(2):293-9. [DOI:10.1038/ki.2012.384] [PMID] [PMCID]

[17] Trivedi M, Pasari A, Chowdhury AR, Kurien AA, Pandey R. The epidemiology, clinical features, and outcome of infection-related glomerulonephritis from East India: A single center experience. Indian J Nephrol. 2017; 27(4):307-12. [DOI:10.4103/ijn.IJN_280_16] [PMID] [PMCID]