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CASE REPORT

IgA Dominant Infection Related Glomerulonephritis Mimicking Primary IgA Nephropathy in Methicillin-Sensitive *Staphylococcus aureus* Osteomyelitis

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Abstract: IgA-dominant infection-related glomerulonephritis (IgA-IRGN) is a histopathological variant of staphylococcus-associated glomerulonephritis (SAGN) that occurs as a result of an immune response to *S. aureus* antigens, with subsequent deposition of IgA in the nephron. This can lead to acute kidney injury, hematuria, and proteinuria. It is important to differentiate IgAIRGN from primary IgA nephropathy (IgAN) because the treatment strategies differ. IgA-dominant IRGN requires treatment of the infection with antibiotics, whereas treatment of primary IgAN involves immunosuppression. Here, we present a case that highlights the clinical dilemma of distinguishing IgA nephropathy from IRGN. Our patient presented with chronic osteomyelitis secondary to Staph. The hospital course was complicated by acute renal failure that required dialysis. Renal biopsy showed IgA deposits, and the patient was initially treated with steroids for IgA Nephropathy. The patient did not respond to immunosuppressive treatments and had a second biopsy, clinical history, and course that closely resembled IgA-IRGN. The patient was eventually removed from dialysis after five months. In patients with documented *S. aureus* infection who present with acute kidney injury, hematuria, and proteinuria, IgA-IRGN should be considered as the etiology. Source control measures should be attempted when necessary and patients should be treated with an appropriate course of antibiotics. Proper diagnosis is important to avoid exposure to immunosuppressive medications and potentially worse outcomes in these patients.

Keywords: – IgA Nephropathy, infection related glomerulonephritis, acute kidney injury

Introduction

Acute kidney injury (AKI) is frequently observed in patients with infections as well as post surgery. There are several different etiologies and pathophysiological mechanisms involved in AKI, which can vary in severity.

Infections more often involve glomeruli, which cause glomerular hematuria and proteinuria, whereas surgical procedures predominantly cause tubulointerstitial damage, often without any urinary abnormalities observed on urinalysis.

This report describes a case involving glomerular and tubulointerstitial damage after right below-knee amputation for severe methicillin-sensitive *Staphylococcus aureus* deep-wound infection.

The pathogenesis of IgA nephropathy and IgA IRGN differs. Differentiating IgA infection related GN (IgA IRGN) and primary IgA nephropathy relies on clinical context, histopathological features including immunofluorescence (IF) patterns.[1–3]

IgA dominant infection related GN is mostly in setting of active infection with acute presentation which resolves with treatment of underlying infection while primary IgA nephropathy hematuria may be synpharyngitic with often chronic incidental discovery and is a progressive disease.[1–3]

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Histopathologically IgA IRGN shows endocapillary proliferation with prominent neutrophil infiltration with sub-epithelial humps whereas primary IgA nephropathy commonly demonstrates mesangial proliferation without significant neutrophil infiltration.

On IF IgA IRGN typically has codominant IgA and C3 staining.

Consequently, the treatments for the two differ and may be at odds.[4] It has been proposed that IgA-IRGN arises from staphylococcal enterotoxins, which act as superantigens that activate T cells.[5] T cell activation and subsequent cytokine release result in polyclonal B cell activation, leading to IgA immune complex deposition.[6] This case report describes a patient with MSSA (Methicillin Sensitive staph aureus) osteomyelitis who presented with IgA-IRGN.

Case Presentation

A 74-year-old man in southwestern United states of America with a history of type 2 diabetes mellitus, hypertension, and baseline Cr of 0.65 underwent right below-knee amputation for a large open necrotic wound in 2024. Wound culture grew methicillin-sensitive *Staphylococcus aureus* (MSSA), which was treated with vancomycin and ceftriaxone, and then narrowed down to cefazolin according to sensitivity.

On admission, his BUN were 11 and creatinine 0.8, respectively. The day before surgery, the patient developed acute kidney injury (AKI). BUN increased to 34 and creatinine to 1.28 and kept rising thereafter, with a constantly increasing BUN/Cr ratio. Urinalysis using a Foley catheter revealed microscopic hematuria, leukocyturia, and proteinuria. The urine protein-to-creatinine ratio 6 days post surgery was 6,493 mg/g, which increased to 18,094 mg/g. Serum creatinine kept rising from 1.28 mg/dl and BUN 34 mg/dl to creatinine 3.5 mg/dl and BUN 173 mg/dl, which prompted hemodialysis (HD) initiation for progressive AKI with uremic symptoms.

Serological evaluation was negative for low C3 and C4 levels, anti-GBM, and ANCA. The patient developed a rash on his hands, which raised the suspicion of vasculitis; thus, a renal biopsy was performed.

The report described 34 glomeruli, 8 with global and 2 with segmental sclerosis, mesangial and endocapillary proliferation, 3 glomeruli with cellular crescents, focal podocyte effacement, ATN, and focal interstitial infiltrate predominantly with lymphocytes and plasma cells, and scattered neutrophils and eosinophils. (Figure 1)

Because of the severity of inflammation, source of infection control, and completion of the antibiotic course, the patient was treated with methylprednisolone pulses (1 g daily for 3 days), followed by oral steroid tapering, which was discontinued on day 17 because of the difficulty in controlling hyperglycemia and the potential utility of steroids.

The patient had a urine output of approximately 1.5 L/day while on steroids, became oliguric and finally anuric within a few days after steroid discontinuation, and was kept on dialysis.

Because there was no improvement in renal function at 6 weeks, another renal biopsy was performed and reviewed by a nephropathologist. In summary, less glomerular inflammation, persistent ATN, increased interstitial fibrosis, and tubular atrophy were observed. (Figure 2) As the inflammation significantly improved, no further steroid treatment was attempted. Renal function continued to improve, and hemodialysis was discontinued after four months. Creatinine level was 2.2 and eGFR 30 was 9 months after the onset of AKI. The urine albumin-creatinine ratio was still within the nephrotic range of 4065 mg/g. The patient's serum albumin level was 3.2 g/dl.

Discussion

This case demonstrates the importance of differentiating primary IgAN from IgA-IRGN. Renal biopsy did not reveal any subendothelial or subepithelial immune deposits, which are considered classic infection-related GN. The only deposits were in the mesangium, which significantly decreased on following renal biopsy. This picture was unusual for severe infection-induced IgA glomerulonephritis. Thus, the initial biopsy report described IgA nephropathy.

Immunosuppressive treatment is an important hallmark of the management of IgAN. Conversely, source control and an appropriate course of antibiotics are recommended treatments for IgA-IRGN.[7]

Although there is a paucity of prospective treatment data, the absence of immunocompromised states has been correlated with complete remission of IgA-IRGN.[4] Similarly, retrospective data have shown that immunosuppressed patients with IgA-IRGN or SAGN (Staph Aureus GN) who were given immunosuppression had higher rates of mortality, end-stage kidney disease, and lower rates of remission.[6] This finding suggests that immunosuppression should be used

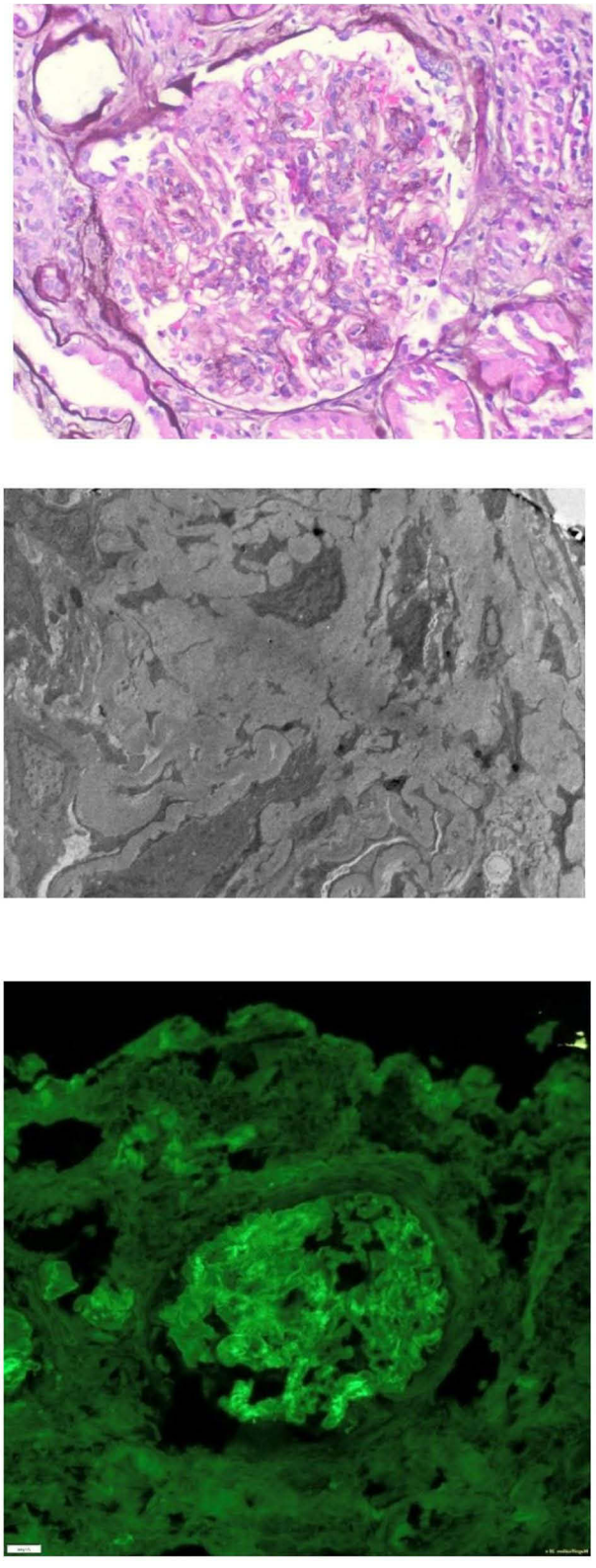

Figure 1 Renal biopsy 15 days post-surgery. (**Top**) Light microscopy - Sample of up to 34 glomeruli, of which 8 glomeruli per level (23%) are globally sclerosed. There are three glomeruli with cellular crescents. There are two glomeruli with segmental sclerosis. There is mild interstitial fibrosis and tubular atrophy involving approximately 20% of sampled cortex. There is diffuse attenuation of the proximal tubulointerstitial cells with cytoplasmic sloughing and loss of the brush borders. There is focal interstitial inflammation composed predominantly of lymphocytes and plasma cells with scattered eosinophils and neutrophils. (**Middle**) Electron microscopy - Ultrastructural evaluations of the glomerulus demonstrates thickening of the glomerular basement membranes. There are frequent mesangial electron dense deposits. (**Bottom**) Immunofluorescence microscopy - On a scale of 0–4+ there is granular mesangial and focal capillary wall staining for IgA (2+), C3 (2+), kappa (2+) and lambda (trace) light chains.

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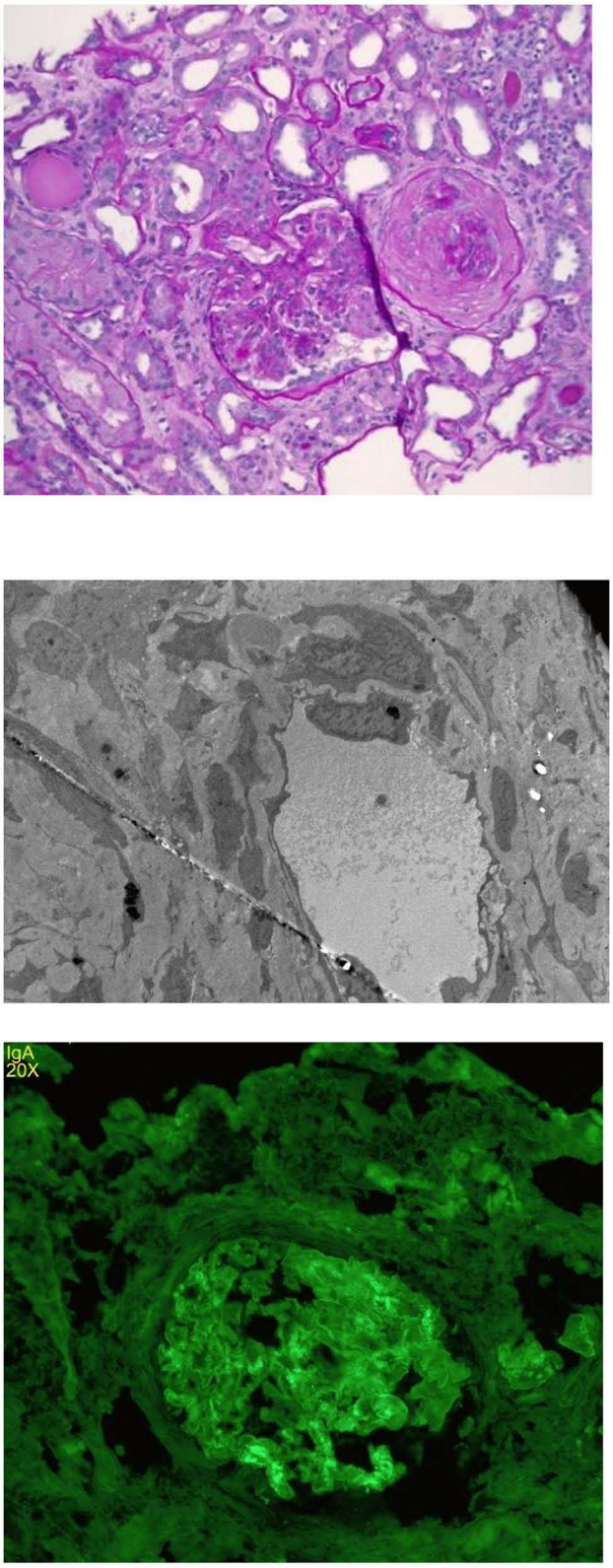

Figure 2 Second biopsy after 6 weeks. (**Top**) Light microscopy - There is segmental glomerulosclerosis periglomerular fibrosis and fibrous crescent formation. There is multifocal acute tubular injury and necrosis. The is increase in tubulointerstitial fibrosis. (**Middle**) Electron microscopy – The Glomerular basement membrane shows segmental thickening and corrugation. There is patchy effacement of foot processes. There is few mesangial electron dense deposits. (**Bottom**) Immunofluorescence microscopy – Granular mesangial and glomerular basement staining for c3 (Trace 1+), IgA (1+), Kappa (trace 1+) and lambda (trace) light chains.

with caution in patients with IgA IRGN. Immunosuppressants can have harmful effects in patient with an already active infection and may be further detrimental to the patient and thus correct diagnosis and treatment is essential.

Retrospective single center study by Huang et al (2021) showed that compared to primary IgAN, patients with IgA-IRGN had higher proportion of crescents, higher proportion of endocapillary hypercellularity and worse prognosis.[8]

In patients with diabetes presenting with hematuria, proteinuria, and acute kidney injury as well as a confirmed wound culture or blood culture of *S Aureus*, SAGN should be considered in the differential diagnosis. Immunofluorescent staining positive for IgA should allow IgA-IRGN to be considered an important morphologic variant.[6,9]

The presentation of IgA-IRGN is similar to that of SAGN, as both can rapidly progress to glomerulonephritis, with varying degrees of proteinuria and hematuria. Proteinuria is common in the nephrotic range, and hematuria is often microscopic,5]. Epidemiological data pertaining to IgA IRGN is lacking. However, in at least one review, the mean age at the time of diagnosis was 54.7 years. There was also a predominance of male patients (74.5%[2)]. Diabetes is a known risk factor for IgA-IRGN and is correlated with unfavorable prognosis.[5,10]

The current literature varies widely on the histological findings of IgA-IRGN[6,7] Common histological reports of IgA-IRGN include the presence of exudative glomerulonephritis with endocapillary proliferation.[4] Other common histological findings of IgA-IRGN include immunofluorescence staining of C3, which is codominant or stronger than that of IgA, and dense subendothelial or mesangial deposits on electron microscopy.[7]

Furthermore, the presence of C3 deposition has been repeatedly supported in the literature in patients with IgA-IRGN and can help elucidate the diagnosis.[7,9,11] As observed in this patient, the histological diagnosis of IgA-IRGN can be confounded by its close resemblance to primary IgAN. However, an accurate historical timeline in conjunction with biopsy can aid in diagnosis.

Laboratory findings for IgA-IRGN also vary and are nonspecific. Given that pathogenesis requires a present infection, there is often an elevated serum white blood cell count, erythrocyte sedimentation rate, and C-reactive protein.[6] Serum IgA levels may be elevated, and C3 levels may decrease; however, no laboratory values are specific to IgA-IRGN.[6]

The prognosis for IgA-IRGN is mixed following treatment with antibiotics; 54.5% of patients experience kidney recovery, 11.7% have persistent kidney dysfunction, and 19.5% progress to end-stage kidney disease. In one case series[7], 14.3%) died. Increased age and diabetes are independent risk factors for an unfavorable prognosis.[6,10,12]

Given the wide degree of variation in both the laboratory and histological findings of IgA-IRGN and its close resemblance to primary IgAN, attention to the disease course must be considered during diagnosis. In patients with acute kidney injury, paroxysmal nephrotic-range proteinuria, and a known source of *S. aureus* infection, IgA-IRGN should be favored over primary IgA nephropathy[13] Additionally, the variability of histological findings may be due to the timing of biopsy in relation to the phase of IgA-IRGN. The acute phase may be subclinical; thus, a biopsy is performed after the initial insults occur.[14]

In our patient, the presence of glomerular capillary staining for IgA and C3, as well as the codominant granular mesangial pattern of IgA and C3, was a subtle finding that supports IgA-IRGN.

Although *S. aureus* is classically described as the culprit of IgA-IRGN owing to the presence of unique enterotoxins, other bacteria and viruses have also been described recently in patients with IgA-IRGN. These include *Streptococcus, Enterobacter, Rickettsia, Chlamydia pneumoniae*, and the hepatitis A virus.[6,7,12,15]

Conclusion

This case report highlights the difficulty in distinguishing between primary IgAN and IgA IRGN. This patient presented with symptoms of SAGN, including kidney injury, hematuria, nephrotic-range proteinuria, and documented *S. aureus* osteomyelitis. However, a biopsy showing mesangial IgA deposits with a normal complement confounded the diagnosis. Distinguishing between these two processes would require greater exposure because treatment for primary IgAN with immunosuppression has been shown to have unfavorable outcomes in patients with SAGN and IgA-IRGN. Early treatment of infection is the mainstay of treatment. Additionally, patients with diabetes are at a greater risk of developing IgA-IRGN, and the use of corticosteroids in these patients can lead to intolerable metabolic side effects.

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Consent

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Disclosure

The authors declare no competing interests.

References

1. Stoneman S, Teh JW, O'Shaughnessy MM. IgA nephropathy in adults: a review. *JAMA*. 2026;335(9):799–813. doi:10.1001/jama.2025.25020
2. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int*, 2021; 100(4S):S1–S276. doi:10.1016/j.kint.2021.05.021
3. Trimarchi H, Coppo R. Glomerular endothelial activation, C4d deposits and microangiopathy in immunoglobulin A nephropathy. *Nephrol Dial Transplant*. 2021;36(4):581–586. doi:10.1093/ndt/gfz241
4. 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
5. Koyama A, Kobayashi M, Yamaguchi N, et al. Glomerulonephritis associated with MRSA infection: a possible role of bacterial superantigen. *Kidney Int*. 1995;47(1):207–216. doi:10.1038/ki.1995.25
6. Takayasu M, Hirayama K, Shimohata H, Kobayashi M, Koyama A. *Staphylococcus aureus* infection-related glomerulonephritis with dominant IgA deposition. *Int J Mole Sci*. 2022;23(13):7482. doi:10.3390/ijms23137482
7. Nasr SH, D'Agati VD. IgA-dominant postinfectious glomerulonephritis: a new twist on an old disease. *Nephron Clin Pract*. 2011;119(1):c18–c26. doi:10.1159/000324180
8. Huang Z, Chen B, Zhou Y, et al. Clinicopathological and prognostic study of IgA-dominant postinfectious glomerulonephritis. *BMC Nephrol*. 2021;22(1):248. doi:10.1186/s12882-021-02462-3
9. Brodsky SV, Nadasdy T, Cassol C, Satoskar A. IgA staining patterns differentiate between IgA nephropathy and IgA-dominant infection-associated glomerulonephritis. *Kidney Int Rep*. 2020;5(6):909–911. doi:10.1016/j.ekir.2020.03.029
10. Wang S-Y, Bu R, Zhang Q, et al. Clinical, pathological, and prognostic characteristics of glomerulonephritis related to staphylococcal infection. *Medicine*. 2016;95(15):e3386. doi:10.1097/MD.0000000000003386
11. Satoskar AA, Molenda M, Scipio P, et al. Henoch-Schönlein purpura-like presentation in IgA-dominant Staphylococcus infectionassociated glomerulonephritis – a diagnostic pitfall. *Clin Nephrol*. 2013;79(4):302–312. doi:10.5414/CN107756. Scipio, Patrice [added].
12. Bu R, Li Q, Duan Z-Y, 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
13. Satoskar AA, Nadasdy G, Plaza JA, et al. Staphylococcus infection-associated glomerulonephritis mimicking IgA nephropathy. *Clin J Am Soc Nephrol*. 2006;1(6):1179–1186. doi:10.2215/CJN.01030306
14. Koo TY, Kim G-H, Park MH. Clinicopathologic features of IgA-dominant postinfectious glomerulonephritis. *Korean J Pathology*. 2012;46 (2):105–114. doi:10.4132/KoreanJPathol.2012.46.2.105
15. Han SH, Kang EW, Kie JH, et al. Spontaneous remission of IgA nephropathy associated with resolution of hepatitis A. *Am J Kidney Dis*. 2010;56 (6):1163–1167. doi:10.1053/j.ajkd.2010.08.018