Staphylococcus Infection–Associated Glomerulonephritis in a Kidney Transplant Patient: Case Report

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ABSTRACT

Background. *Staphylococcus* infection–associated glomerulonephritis is a rare cause of graft dysfunction in kidney transplant. Suspicion should be high in the setting of elevation of serum creatinine, active urinary sediment, with or without hypocomplementemia, and simultaneous *Staphylococcus aureus* infection. A kidney biopsy is usually diagnostic.

Case Report. A 56-year-old man, who received a kidney transplant in 1998, with basal serum creatinine of 1.2 mg/dL and normal urinary sediment, was admitted to our kidney transplantation unit with graft dysfunction and a urinary tract infection caused by *S aureus* with septicemia, treated with antibiotics, in the context of recently intensified immunosuppression for a primary immune thrombocytopenia diagnosed 3 weeks earlier. After antibiotic treatment, the patient persisted with graft dysfunction, edema, and hypertension, with a *S aureus* isolation in the urine culture, active urinary sediment, and low C3. A kidney biopsy was performed, showing diffuse proliferative endocapillary and mesangial glomerulonephritis, with IgA(++) and C3(++) mesangial and endocapillary deposits in immunofluorescence. The patient was treated symptomatically and maintained his regular immunosuppression. At the last follow-up, his serum creatinine value was stable at 2.5 mg/dL.

Conclusions. The onset of a nephritic syndrome with a simultaneous *S aureus* infection should lead to suspicion of this uncommon entity, confirmed histologically. Despite its association with poor graft survival, our patient's graft survival remained stable.

REGARDING bacterial infections and the development of glomerulonephritis (GN), 2 different entities should be considered: a postinfectious GN and a GN with active ongoing infection. "Post" means that the infection is gone (eg, poststreptococcal GN), which is not seen in most cases of *Staphylococcus* infection–associated GN (SIAGN). Also, in postinfectious GN, the latent period is usually 1–4 weeks, whereas the term "GN with active ongoing infection" means that there is a SIAGN (usually IgA dominant) or a GN with other persistent infections (endocarditis, deep-seated abscesses, shunt nephritis, cellulitis in an ischemic extremity, osteomyelitis, diabetic foot ulcers, cellulitis, pneumonia, infected surgical sites, visceral abscess, septic arthritis, infected pacemaker, indwelling catheters, intravenous lines, infected abdominal mesh, dental infection, etc). The latter may last weeks and its source is variable, because there are many different bacterial, viral, fungal, and parasitic infections that can cause it [1]. Therefore, the term postinfectious is a misnomer and should not be used [2].

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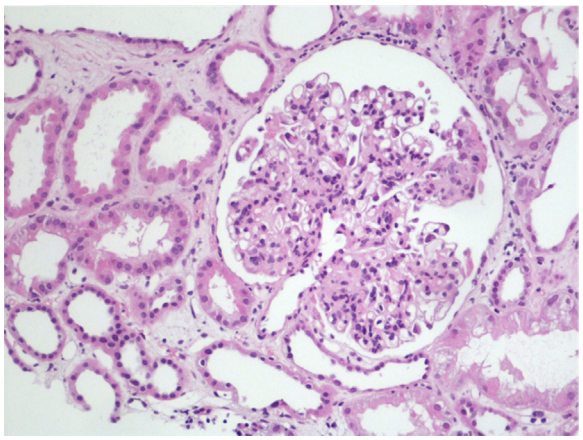

Fig 1. Kidney biopsy showing diffuse endocapillary mesangial proliferation (hematoxylin and eosin).

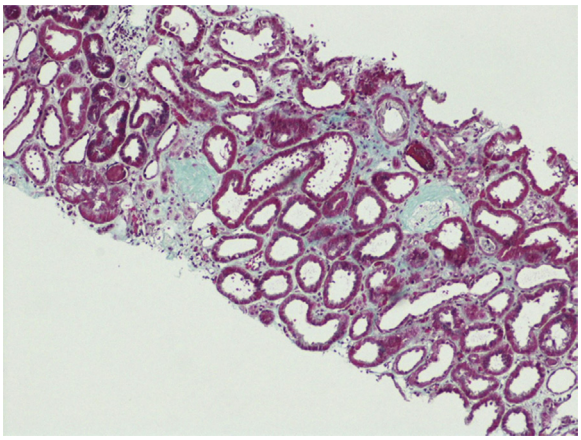

Fig 2. Kidney biopsy showing interstitial fibrosis (Masson trichrome stain).

In developed countries, the incidence of poststreptococcal GN has declined owing to the of successful treatment of acute streptococcal infections. Meanwhile, SIAGN is on the rise because of emerging drug-resistant strains of *Staphylococcus* and both nosocomial and community-acquired staphylococcal infections as well as because of the growing elderly population with increasing prevalence of comorbidities, such as diabetes and morbid obesity.

SIAGN is mediated by immune complexes and a rare cause of graft dysfunction in kidney transplants. IgA-dominant or codominant immune complexes are commonly seen, posing a diagnostic pitfall with idiopathic IgA nephropathy (and Henoch-Schönlein purpura) [1]. The antigen component of the immune complex is derived from the infective agent, similarly to poststreptococcal GN [3]. Still, the pathophysiology of this entity remains largely unknown. It most likely involves glomerular deposition of preformed circulating immune complexes or in situ immune complex formation due to cationic staphylococcal antigens planted in the glomeruli [4–6].

SIAGN should be suspected when there are signs of acute kidney injury, hematuria or proteinuria, or hypocomplementemia in the setting of culture-proven ongoing *S aureus* infection. A complete clinical nephritic syndrome may occur.

Unlike poststreptococcal GN, upper respiratory tract infection is not usually a cause of SIAGN. The renal prognosis is much worse in the latter, particularly in patients with underlying diabetic nephropathy. Cutaneous vasculitis can occur in patients with SIAGN, imitating Henoch-Schönlein purpura (IgA vasculitis) or antineutrophil cytoplasmic antibody–associated vasculitis [2,7], which is not a manifestation of poststreptococcal GN.

The kidney biopsy is usually diagnostic and it may show a GN with endo- or extracapillary proliferation, frequently with visible IgA or IgG deposits codominant with C3 deposits, visible with the use of immunofluorescence.

CASE REPORT

A 56-year-old man with chronic kidney disease, who underwent kidney transplantation in December 1998 and had as other relevant comorbidities arterial hypertension and primary autoimmune thrombocytopenia, presented a basal creatinine of 1.2 mg/dL and a normal urinary sediment in routine post-transplantation consultations. The patient was admitted in the kidney transplantation unit in May 2016 for kidney graft dysfunction (serum creatinine, 3.07 mg/dL), in the setting of immunosuppression intensification for the treatment of a primary immune thrombocytopenia (125 mg cyclosporine twice daily and 40 mg prednisolone once daily) diagnosed 3 weeks earlier by the hematology department. Kidney graft pyelonephritis was clinically suspected, with bacteremia (positive blood cultures for *S aureus*, sensitive to gentamicin, sulfamethoxazole/trimethoprim, and oxacillin and resistant to penicillin G), treated empirically before the antibiotic-sensitivity testing with 600 mg linezolid twice daily for 10 days. A urine culture was

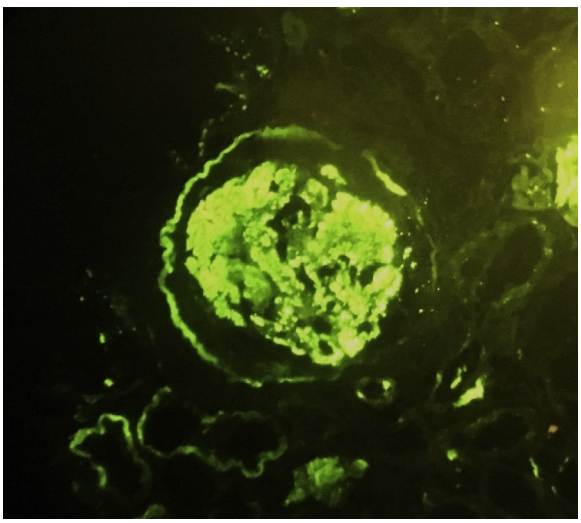

Fig 3. Immunofluorescence showing C3 deposition in the capillary wall and mesangium.