Kidney Injury in a Patient with Hypocomplementemia and Diffuse Lymphadenopathy

Anam Rehan

Case Description
A 76-year-old Peruvian man presented with complaints of dysuria and was noted to have elevated serum creatinine. The patient had no prior history of kidney disease. Past medical history was only notable for chronic low back pain, anxiety, and prostate cancer status post prostatectomy without chemoradiation. The patient denied ingestion of nonsteroidal anti-

Figure 1. Key kidney biopsy findings for IgG-4 related tubulointerstitial nephritis. (A) Dense infiltrate of plasma cells and lymphocytes as seen on light microscopy (hematoxylin and eosin stain). (B) Storiform fibrosis with “cartwheel” appearance is observed on light microscopy (hematoxylin and eosin stain). (C) IgG4 positive cells are observed in greater than 10 cells per high power field (IgG4 immunostain).

Yale School of Medicine, New Haven, Connecticut

Correspondence: Dr. Anam Rehan, Yale School of Medicine, 330 Cedar Street, New Haven, CT 06520. Email: anam.rehan@yale.edu
inflammatory drugs, herbal supplements, over-the-counter medications or proton pump inhibitors. All other constitutional symptoms and pertinent family history were negative. Outside of an elevated blood pressure, the physical examination was unremarkable.

Electrolytes were normal while blood urea nitrogen was 49 mg/dl and serum creatinine was 3.1 mg/dl. Hemoglobin was 10.2 g/dl and hematocrit was 30.9% with no thrombocytopenia or eosinophilia. All other laboratory tests were unremarkable. Serologic work-up showed hypocomplementemia (C3: 50 mg/dl; C4: 2 mg/dl) and positive anti-nuclear antibody (1:320, dense and speckled). Computed tomography scan did not demonstrate nephrolithiasis but showed enlarged lymph nodes in the retroperitoneum, pelvis, right hilar, mediastinum, left axilla and retroperitoneal area. Pulmonary ground glass opacities were also observed.

Urinalysis showed 1+ protein but was otherwise negative. Ultrasound showed bilateral 10.6 cm kidneys with normal cortical echogenicity. Kidney biopsy showed severe, diffuse interstitial infiltrate consisting of lymphocytes and plasma cells involving >70% of the interstitium (Figure 1A). Storiform fibrosis was also observed in the interstitium (Figure 1B). Based on these findings, immunostaining for IgG and IgG4 was undertaken and demonstrated focal areas with >10 IgG4+ plasma cells/high power field (Figure 1C). This combination of findings was considered consistent with a diagnosis of IgG4-related tubulointerstitial nephritis.

IgG4-related disease is an immune-mediated condition that can cause fibroinflammatory lesions in any organ including the kidneys (1). The clinical presentation including multiorgan involvement can mimic malignancy, infection, and other rheumatologic manifestations. Organs that may be involved include the salivary glands, pancreas and biliary tree, lungs, kidneys, infrarenal aorta, retroperitoneum, lymph nodes, meninges, and thyroid gland. Blood tests sometimes demonstrated hypocomplementemia and elevated IgG4 levels. Radiologic findings such as a sausage-shaped pancreas, infrarenal periaortitis, and masses in the lungs and kidneys are strongly suggestive of IgG4 disease. The kidneys can be involved with masses, retroperitoneal lymphadenopathy with obstruction, and tubulointerstitial nephritis. The characteristic pathologic findings include a lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis and IgG4+ plasma cell infiltrates. However, obliterative phlebitis and storiform fibrosis may not always be observed with IgG4 disease. Management of IgG4-related tubulointerstitial nephritis consists primarily of corticosteroid therapy. Corticosteroids are often quite effective; however, relapse can occur during drug taper. In cases resistant to corticosteroids, rituximab has been successful (2). Despite good treatment response, neither approach has been seen to cure the disease (3). Therefore, it is recommended that these patients have close monitoring of their kidney function and urinalyses after completion of therapy.

**Teaching Points**
- IgG4-related disease is immune mediated with involvement of virtually any organ with fibroinflammatory lesions.
- Tubulointerstitial nephritis is one of the kidney manifestations of IgG4-related disease. Retroperitoneal disease with obstruction and masses within the kidneys are other manifestations.
- Histology reveals a lymphoplasmacytic dominant interstitial infiltrate with significant IgG4 positive cell staining. Storiform fibrosis and obliterative phlebitis may be observed.

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The author has nothing to disclose.

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**Author Contributions**
A. Rehan conceptualized the study, wrote the original draft, and reviewed and edited the manuscript.

**References**

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