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On the Cover

What’s the diagnosis?

Case description:
A 55-year-old woman with AIDS presented with anorexia, vomiting and weight loss. Two months prior she initiated antiretroviral therapy and treatment for disseminated \textit{Mycobacterium tuberculosis} (Mtb). Labs revealed acute kidney injury, serum creatinine (SCr) of 1.5 mg/dL from 0.7 mg/dL over 6 weeks, and subnephrotic-range proteinuria (2.8 g/dL). Urine microscopy showed granular casts and red and white blood cells without bacteria. Urine, blood and sputum cultures for acid-fast bacilli (AFB) were negative. Renal ultrasound was unremarkable and computerized tomography demonstrated improvement in both pulmonary opacities and thoracic and retroperitoneal lymphadenopathy. Immune reconstitution inflammatory syndrome (IRIS) was suspected and a short course of steroids was given. SCr initially improved but then worsened, prompting a kidney biopsy.

Images:
- Left panel: The cortex shows a granulomatous interstitial nephritis (GIN) with poorly formed, coalescing granulomas composed of epithelioid histiocytes and occasional multinucleated giant cells, with an associated lymphoplasmacytic inflammatory infiltrate. There is no necrosis or significant neutrophilic or eosinophilic inflammation. The glomeruli are normal.
- Right panel: Multiple AFB identified within granulomas with a focal beaded appearance on AFB stain.

Teaching points:
- The histological differential diagnosis for GIN includes drug-induced, sarcoidosis, deposition of crystals or other foreign material, infection, granulomatosis with polyangiitis, tubulointerstitial nephritis with uveitis and IRIS.
- IRIS-related kidney disease was considered. IRIS is an inflammatory disorder characterized by paradoxical worsening during immune recovery of manifestations of pre-existing opportunistic infections, which generally responds to steroids. Although renal injury from IRIS is rare, \textit{Mycobacterium} is the main associated infection. Renal biopsy in patients with IRIS demonstrates noncaseating GIN without microorganisms.
- In this case, the GIN is associated with AFB, which most likely represents Mtb given their morphology and the clinical history of previous disseminated Mtb infection. Sterile pyuria and hematuria can be seen. The kidneys are common targets when Mtb hematogenously disseminates. Treatment consists of continuing Mtb therapy for a full nine months.

(Images and text provided by Kelly Mazurek, Nicole Andeen, Roberto Nicosia, and Leah Haseley, University of Washington, Seattle, Washington)