AKI and Hypercalcemia in a Patient with Weakness and Fatigue

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Case Description
A 59-year-old, Black patient presented to the emergency department for fatigue and weakness lasting for several weeks. Past medical history was significant for hypertension and migraine headaches. Physical exam was nonfocal, with normal breath sounds, no peripheral lymphadenopathy, no rash, and no edema. Laboratory findings included BUN of 40 mg/dl (7–20 mg/dl), creatinine of 4.16 mg/dl (0.6–1.2 mg/dl), serum calcium of 12.4 mg/dl (8.5–10.5 mg/dl), eGFR of 15 ml/min per 1.73 m² (>60 ml/min per 1.73 m²), parathyroid hormone <3 pg/ml (10–65 pg/ml), 1,25-dihydroxyvitamin D of 72 ng/ml (25–40 ng/ml), and angiotensin-converting enzyme of 112 U/L (8–53 U/L). Head computed tomography scan and chest x-ray were unremarkable. Serologic studies, including cerebral spinal fluid analysis, were negative for malignancy. The elevated angiotensin-converting enzyme and 1,25-dihydroxyvitamin D levels made sarcoid a strong possibility. A kidney biopsy was performed to determine the cause of AKI.

The kidney biopsy specimen (Figure 1A) demonstrated granulomatous interstitial nephritis with widespread, coalescing, non-necrotizing granulomas, with occasional multinucleated giant cells in a background of lymphocytes, plasma cells, and eosinophils. No acid-fast or fungal organisms were identified on special stains. Some tubules showed prominent droplets within their cytoplasm, highlighted by lysozyme stain. Glomeruli and vessels were without morphologic abnormalities, and immunofluorescence studies were negative. Taken together with the clinical scenario, a diagnosis of sarcoid-related tubulointerstitial nephritis was made.

The patient was subsequently started on a 10-week corticosteroid regimen. Symptoms of weakness and fatigue resolved and, at 6-week follow-up, laboratory values were as follows: calcium of 9.9 mg/dl (8.5–10.5 mg/dl), BUN of 26 mg/dl (7–20 mg/dl), creatinine of 1.45 mg/dl (0.6–1.2 mg/dl), and eGFR of 50 ml/min per 1.73 m² (>60 ml/min per 1.73 m²).

Sarcoidosis is an idiopathic, chronic, systemic disease characterized by the formation of non-necrotizing granulomas in various organs. Sarcoidosis can involve any organ but, in >90% of patients, it manifests with pulmonary involvement (1). Renal-limited sarcoidosis, as seen in this patient, is uncommon, and primarily documented in case reports (2). Although the etiology of sarcoidosis and renal involvement is unknown, the majority of sarcoid-related renal failure is due to nephrocaldinosis, with or without nephrolithiasis, or interstitial nephritis, with or without granulomas (3).

Lysozyme staining of proximal tubules on kidney biopsy specimens, as seen in this case, may help discriminate sarcoidosis from other causes of tubulointerstitial nephritis (4). Lysozome is produced by monocyte-lineage cells—including macrophages, which comprise granulomas—and resolved by proximal tubules. Lysozyme-induced nephropathy is characterized by acute tubular injury with cytoplasmic inclusions that stain for lysozyme and have an ultrastructural appearance of autophagosomes. This entity may be seen in patients with chronic monocytic and myelomonocytic leukemia (5).

In summary, we present a patient with renal-limited sarcoidosis presenting with fatigue and classic laboratory findings without pulmonary involvement. The kidney biopsy sample with lysozyme staining supported a diagnosis of sarcoid-related tubulointerstitial nephritis, and the patient had an excellent response to corticosteroids.

Teaching Points
- Sarcoidosis is a chronic disease that can affect any organ, although pulmonary involvement is involved in >90% of cases.
- Symptoms of weakness and fatigue, in addition to AKI and hypercalcemia, may be seen in patients with sarcoid-related tubulointerstitial nephritis.
- Lysozyme staining of proximal tubules may be a useful ancillary tool to distinguish sarcoid-related tubulointerstitial nephritis from other causes of tubulointerstitial nephritis.

Disclosures
M. Stroemel reports receiving personal fees from the Veterans Administration, during the conduct of the study. M. Stroemel also reports receiving a monthly stipend from Fresenius Medical Care of North America to serve as medical director at a local dialysis clinic to monitor quality, outcomes, and ensure regulatory compliance. All remaining authors have nothing to disclose.

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Author Contributions
N. Andeen was responsible for methodology and visualization; N. Andeen, C. Rahimi, and M. Stroemel conceptualized the study, wrote the original draft, and reviewed and edited the manuscript; and N. Andeen and M. Stroemel were responsible for resources, supervision, and validation.

References

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Figure 1. | Kidney biopsy specimens. (A) Kidney biopsy specimen demonstrated granulomatous interstitial nephritis. Stained with Periodic acid–Schiff. Original magnification, ×200. (B) Lysozyme stain highlighted tubules and non-necrotizing granulomas. Original magnification, ×200.