Severe AKI in a Patient on Multiple Antimicrobial Agents for Leg Infection

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Case Description
A 47-year-old man with no significant past medical history presented with fever and pain over his right leg. The patient was recently hospitalized 2 months previously after suffering a traumatic right leg injury requiring intramedullary nail insertion. The hardware contained antibiotic cement (vancomycin, gentamicin, and tobramycin). Unfortunately, the hospital course was complicated by postoperative surgical site infection. Candida albicans, Enterococcus faecalis, and coagulase negative Staphylococcus were noted on deep-tissue cultures. The patient underwent surgical drainage and treated with intravenous vancomycin and piperacillin-tazobactam and oral fluconazole. The patient was subsequently discharged on vancomycin and fluconazole and was readmitted 3 weeks later with concern for wound/hardware infection. The patient underwent further debridement and was treated with intravenous vancomycin and piperacillin-tazobactam. Serum creatinine rose from baseline 0.89 to 3.17 mg/dl and continued to increase to 5.86 mg/dl, prompting nephrology consultation.

Laboratory tests revealed sodium 130 mEq/L, total CO2 20 mEq/L, BUN 27 mg/dl, serum creatinine 5.86 mg/dl, white blood cell count 4.0/μl, hemoglobin 8.4 g/dl, and hematocrit 26%. All other labs were unremarkable. Urinalysis was negative, and urine sediment was bland. Ultrasound revealed 14.1- and 13.9-cm kidneys with mild echogenicity, without hydronephrosis or stones. Vancomycin level was 47.6 mg/L, whereas gentamicin and tobramycin levels were <0.3 mg/L. Kidney biopsy revealed normal glomeruli with diffuse acute tubular injury and focal interstitial infiltrate. Numerous tubular profiles contained casts that had an associated monotypic reaction (Figures 1, A–C). These findings were considered consistent with vancomycin-associated acute tubular injury and cast nephropathy.

Vancomycin is a glycopeptide antibiotic that is widely used to treat Gram-positive organisms resistant to β-lactam antibiotics. Vancomycin nephrotoxicity is rare with standard dosing and therapeutic levels. However, AKI does develop with high doses and supratherapeutic levels, especially when combined with piperacillin-tazobactam (1,2). When AKI occurs in the setting of vancomycin therapy and supratherapeutic levels, patients are presumed to have acute tubular injury and often do not undergo kidney biopsy. When biopsy is undertaken, the histopathology documented in the literature consists primarily of two lesions: acute tubular injury/necrosis and acute interstitial nephritis (3). The lesion known as vancomycin-associated cast nephropathy was first reported in nine patients, eight with supratherapeutic levels (4). CD68+ macrophages surrounded the casts and were present in the interstitium, suggesting that the casts generated an inflammatory process. Transmission electron microscopy with immunogold labeling demonstrated that intratubular casts contained vancomycin aggregates, which appeared as 100- to 900-nm noncrystalline spherules. Using various techniques, the authors demonstrated that these casts contained both vancomycin and uromodulin.

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was discontinued, and the patient subsequently recovered kidney function back to baseline.

Teaching Points
- Vancomycin is associated with AKI in patients with underlying risk factors.
- Acute tubular injury/necrosis and acute interstitial nephritis have not been commonly described on kidney biopsy in patients developing AKI on vancomycin therapy.
- Vancomycin-associated cast nephropathy, which has characteristic histologic findings on light and electron microscopy, appears to be a unique cause of AKI that occurs when vancomycin and uromodulin combine in renal tubular lumens.

Disclosures
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Author Contributions
M.A. Perazella reviewed and edited the manuscript. All authors were responsible for conceptualization and for writing the original draft of the manuscript.

References

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