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

Anam Rehan,1 Gilbert W. Moeckel,2 and Mark A. Perazella1

KIDNEY360 3: 405–406, 2022. doi: https://doi.org/10.34067/KID.0006102021

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 but 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. The patient underwent surgical drainage and 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. The patient described some nausea and lower-extremity edema but denied ingestion of nonsteroidal anti-inflammatory drugs or over-the-counter medication. Vital signs were normal, whereas physical examination was only remarkable for 2+ lower-extremity edema.

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. The lesion was reproduced in four mice (4). A subsequent publication describes the heterogenous nature of this cast in 25 vancomycin-treated patients with mean vancomycin trough levels of 25 mg/L (5). Casts were composed of microparticles of variable sizes, which ranged from finely granular to larger faint globules with a pale center and peripheral condensation. In addition to a variety of cast appearances on light microscopy, electron microscopy also revealed a spectrum of findings, including variably electron-dense round particles or short tubular structures. Individual or aggregated spherules with well-defined smooth contours and circumferential peripheral condensation were also present. Although we did not stain the casts for vancomycin and uromodulin in our case, the intratubular casts appear quite similar to vancomycin-associated casts previously described. Vancomycin

1Section of Nephrology, Yale School of Medicine, New Haven, Connecticut
2Pathology Department, Yale School of Medicine, New Haven, Connecticut

Correspondence: Dr. Mark A. Perazella, Section of Nephrology, Yale School of Medicine, 330 Cedar Street, New Haven, CT 06520.
Email: mark.perazella@yale.edu
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

M.A. Perazella reports honoraria from UpToDate and being a scientific advisor for AJKD, CJASN, Clinical Nephrology, Journal of Onco-Nephrology, Kidney International, KI Reports, and Kidney360. All remaining authors have nothing to disclose.

Funding

None.

Acknowledgments

Informed consent was obtained from the patient.

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


Received: September 20, 2021 Accepted: September 22, 2021