The Case | Acute kidney injury in a patient with *P. carinii* pneumonia

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A 61-year-old man who had undergone remote orthotopic liver transplant was admitted for fever and progressive dyspnea of several days duration. A chest radiograph demonstrated bilateral interstitial infiltrates with diffuse patchy alveolar opacities. The patient was treated empirically for presumed pulmonary infection with broad-spectrum antibiotics. High-dose trimethoprim/sulfamethoxazole was initiated 24 h after admission because of continued fevers and concern for *Pneumocystis carinii* pneumonia. Bronchoscopy was performed and direct fluorescent antibody staining for *Pneumocystis carinii* pneumonia was positive, confirming the diagnosis.

Before admission, the patient carried a diagnosis of chronic kidney disease because of toxicity from calcineurin inhibitors, which had since been discontinued. Seventy-two hours after presentation and despite ongoing intravenous hydration, the patient’s creatinine increased from a baseline of 1.6 mg per 100 ml (122 μmol/l) to 3.4 mg per 100 ml (259 μmol/l), representing a decline in estimated glomerular filtration rate of 42–19 ml/min per 1.73 m². Urine output had also decreased dramatically. Renal ultrasound was unremarkable with no evidence for obstruction. By initial dipstick analysis, the urine had pH of 5.0, specific gravity 1.020, negative blood, trace protein, and negative leukocyte esterase. A microscopic evaluation of the urine sediment demonstrated rare granular casts, no red blood cells, rare white blood cells per high-powered field, and innumerable yellow-brown crystals as depicted (Figure 1).

What is the cause of the patient’s renal failure based on the findings of the urine sediment?

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The Diagnosis | Sulfonamide crystalluria

Although the patient appeared dehydrated, his creatinine worsened despite intravenous saline. No other nephrotoxic agents had been administered, and no evidence suggested acute interstitial nephritis from antimicrobials. We supposed that intratubular obstruction from the observed sulfonamide crystalluria was a significant contributor to the acute kidney injury. The trimethoprim/sulfamethoxazole was replaced with an alternative antimicrobial, and intravenous isotonic sodium bicarbonate was administered for hydration and alkalinization. Within 96 h, the crystalluria resolved (Figure 2), leaving only monomorphic hematuria from the bladder catheter trauma. The patient’s creatinine returned near his baseline to 1.8 mg per 100 ml (137 μmol/l), and he recovered from his respiratory illness to be discharged.

Acute renal failure from sulfonamide crystalluria is reported to occur in 0.4–29% of patients, and typically develops approximately 7 days after drug initiation, although it may be seen sooner. As they are weak acids, sulfonamides crystallize in sufficiently acidic urine (pH < 5.5), causing intratubular obstruction and acute decline in renal function. High doses, such as those used to treat Pneumocystis carinii pneumonia and toxoplasmosis, increase the probability of crystal formation. Hypoalbuminemia and dehydration, which were both present in our patient, also contribute to urinary precipitation of these drugs and their metabolites.1,2

Renal ultrasound may demonstrate echogenic foci in the renal parenchyma or collecting system.3 Crystals are typically amber in color, and their shapes may be needle-shaped, rosettes, dumbbells, or ‘shocks of wheat,’ and may be specific to the sulfonamide-derivative administered.2,4 A Lignin test, in which 10% hydrochloric acid is mixed with urine, produces a yellowish-orange color when sulfa is present,1 allowing detection of these drugs.

Treatment of acute kidney injury from sulfonamide crystalluria is comprised of withdrawal of the drug, hydration and/or diuretics to establish high urine flow, and alkalinization to maintain urine pH > 7.15.1,2 Rarely, ureteral catheterization, nephrostomy tube placement, or even hemodialysis is necessary. Reintroduction or even continuation of the drug may be tolerated with aggressive hydration and urinary alkalinization.1

Patients receiving high doses of sulfonamide to treat opportunistic infections are prone to acute kidney injury from crystalluria. A microscopic analysis of the urine sediment is an inexpensive but essential tool in suggesting this diagnosis. Familiarity with the characteristic appearance of sulfa crystals allows rapid supportive and therapeutic intervention.

REFERENCES