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On the Cover

What's the diagnosis? A 46-year-old woman with history of deceased donor kidney transplant 4 years ago presented with headache and confusion. Workup revealed finding diagnostic of neurotoxoplasmosis. The patient's immunosuppressive regimen was modified she also received intravenous sulfadiazine, pyrimethamine, and folinic acid. Over the next 10 days, she deteriorated with worsening sensorium, mild hypotension, and serum creatinine concentration rising from 1.3 to 1.8 mg/dL. Intravenous fluids restored hemodynamic stability; however kidney function did not improve with serum creatinine rising further to 2.1 mg/dL. Physical examination noted a fluctuating mental status but no other significant abnormalities. Ultrasound of the renal allograft revealed increased echogenicity and high resistive indices. Urinalysis revealed pH 5.5, SG 1.013, trace protein, trace blood, and 1+ leukocyte esterase. Urine microscopy demonstrated 5-8 white blood cells/HPF, and numerous sulfadiazine crystals (cover image), which were birefringent with polarization. Kidney biopsy was not obtained as the patient had evidence of crystalline-related kidney injury. Isotonic sodium bicarbonate intravenous fluids were administered to alkalinize the urine and increase urinary flow rates. Kidney function improved and returned to baseline over the next few days. Sulfadiazine is employed in high doses to treat CNS toxoplasmosis in immunocompromised hosts. Risk of precipitation and AKI increases when the urine pH is less than 5.5 the dose of sulfadiazine is 4g/day or higher. Sulfadiazine crystals can assume many shapes, the most common being needle-shaped crystals, rosettes, and those resembling shocks (sheaves) of wheat as seen on the cover. Intrarenal sulfadiazine precipitation may be prevented by maintaining high urinary flow rates (fluid intake above 3 L/day) and alkalinizing the urine to a pH >7.15 (bicarbonate-containing intravenous fluids), which increases sulfadiazine solubility by more than 20-fold. In patients with severe and established AKI, the bicarbonate infusion should be discontinued if the urine pH does not rise above 7.0 after 12 hours or if volume overload or metabolic alkalosis develops. Hemodialysis offers no benefit for the removal of sulfonamide antibiotics. (*Images and text provided by Jose Antonio Tesser Poloni, Elizete Keitel, MD, and Auria Ferreira dos Santos, MD, Irmandade da Santa Casa de Misericordia de Porto Alegre and Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, Brazil, and Mark A. Perazella, MD, Yale University School of Medicine, New Haven, Connecticut*)