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On the Cover

What's the diagnosis?

Case description:

A 66-year-old man with a history of cirrhosis, ureteral cancer status/post stent placement, aneurysm and coiling of the left renal artery, diabetes and hypertension was admitted to the hospital for pneumonia. Sputum cultures grew *Stenotrophomonas maltophilia*, for which he was initially treated with oral trimethoprim-sulfamethoxazole (TMP-SMX) 400/80 mg x 12 doses and then intravenous TMP-SMX 400 mg x 15 doses. The patient developed acute kidney injury, with a rise in serum creatinine from 0.9 mg/dL on the day of admission to 1.2 mg/dL on the first day of TMP-SMX use, rising to 2.3 mg/dL on day 12 of TMP-SMX. He also developed hyperkalemia to 5.3 mEq/L and a non-anion gap metabolic acidosis, prompting a nephrology consult. Urine was obtained for microscopic analysis, which revealed numerous rhomboid shaped crystals. It was suspected that sulfamethoxazole could be contributing to crystal-induced nephropathy. Sulfamethoxazole was immediately discontinued and intravenous sodium bicarbonate was given to alkalinize the urine. On repeat urine microscopy these crystals disappeared. The patient was diagnosed with crystal-induced nephropathy due to sulfamethoxazole. The patient's kidney function worsened progressively and had to be initiated on dialysis. Fortunately, kidney function gradually recovered and the patient was able to come off of dialysis and serum creatinine went back to baseline.

Image Description:

Urine microscopy demonstrates large triangular to rhomboid shaped crystals. These crystals were birefringent under polarized light microscopy.

Image 1: Triangular sulfamethoxazole crystals, 400X

Image 2: Rhomboid sulfamethoxazole crystals, 100X

Image 3: Triangular sulfamethoxazole crystals under polarized light, 400X

Teaching Points:

Trimethoprim-sulfamethoxazole is a commonly prescribed antibiotic; side effects from trimethoprim include elevation of serum potassium and serum creatinine by inhibition of epithelial sodium channel in the distal nephron, while sulfamethoxazole may cause crystal-induced nephropathy.

- Sulfamethoxazole crystals are formed in an acidic pH and can appear in different shapes including rhomboid, triangular, sheaves of wheat, rosettes or needle-shaped.
- Alkalinization of urine may help increase the solubility of sulfamethoxazole and prevent crystallization.
- Sulfamethoxazole crystals are soluble in acetone; this can help differentiate between uric acid crystals and sulfamethoxazole crystals, as both can appear similar in shape and size, and both show birefringence under polarized light.
- Urine microscopy is an indispensable tool in the diagnostic evaluation of acute kidney injury.
- Our case emphasizes the need to be cognizant about medication-associated side effects, as prompt discontinuation of offending agents may help improve patient outcomes.

Acknowledgements: The patient's family verbally consented to the use of data and imaging for the purpose of this publication. The patient's identity is concealed and all sources of patient identifiers including patient's date of birth, social security number or electronic medical record number are protected and concealed. The chances of breach of confidentiality and patient privacy is not possible and IRB approval was not obtained for this case report.

(Images and text provided by Syed Hassan Raza Bukhari, University of Virginia-Nephrology, Charlottesville, Virginia; Helen Cathro, University of Virginia-Pathology, Charlottesville, Virginia; and Joshua King, University of Virginia-Nephrology and Medical Toxicology) of Virginia-Nephrology and Medical Toxicology