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On the Cover

What's the diagnosis? A 21-year-old woman presented to the Emergency Department with a complaint of acute onset of right flank pain. Exam revealed right flank tenderness, dipstick urinalysis was positive for blood and leukocyte esterase, and CT scan demonstrated a 6 mm stone in the right mid-ureter. Urine microscopy was notable for isomorphic red blood cells, white blood cells and hexagonal crystals (cover image), consistent with cystine. Subsequent stone analysis confirmed cystine as the major component.

Cystinuria is an autosomal recessive genetic cause of kidney stones, which are composed of cystine, a homodimer of the amino acid cysteine, which occurs in 1 in 7000–10,000 births. Several gene mutations have been noted in patients with cystinuria, including mutations in the SLC3A1 and SLC7A9 genes. Mutations in either of these genes disrupt the amino acid transporter protein complex function in the proximal tubule, reducing reabsorption of cystine and other dibasic amino acids.

Cystine stones are found in 1 to 2 percent of stone formers, although a higher percentage (5%) is noted in children with stones. Because it is very difficult to reduce the amount of cystine being excreted, prevention of recurrent cystine stones is aimed at increasing the solubility of cystine in the urine. As the solubility of cystine in urine is pH dependent, an alkaline pH is desired. General recommendations to prevent cystine stone formation include: 1) increased fluid intake, 2) reduced intake of sodium (<50 mmol/day) and protein (0.8–1.0 g/kg per d), and 3) urinary alkalinization (urine pH 7 or greater) with potassium citrate (typically 60–80 mEq/day in 3 divided doses). If these measures are not sufficient, tiopronin, a thiol-containing drug, may reduce stone formation by covalently binding to the cystine molecule and increasing its solubility. Image and text provided by Jose Antonio Tesser Poloni, Irmandade da Santa Casa de Misericordia de Porto Alegre, Porto Alegre, Brazil, and Mark A. Perazella, Yale University School of Medicine.