

Crystalluria

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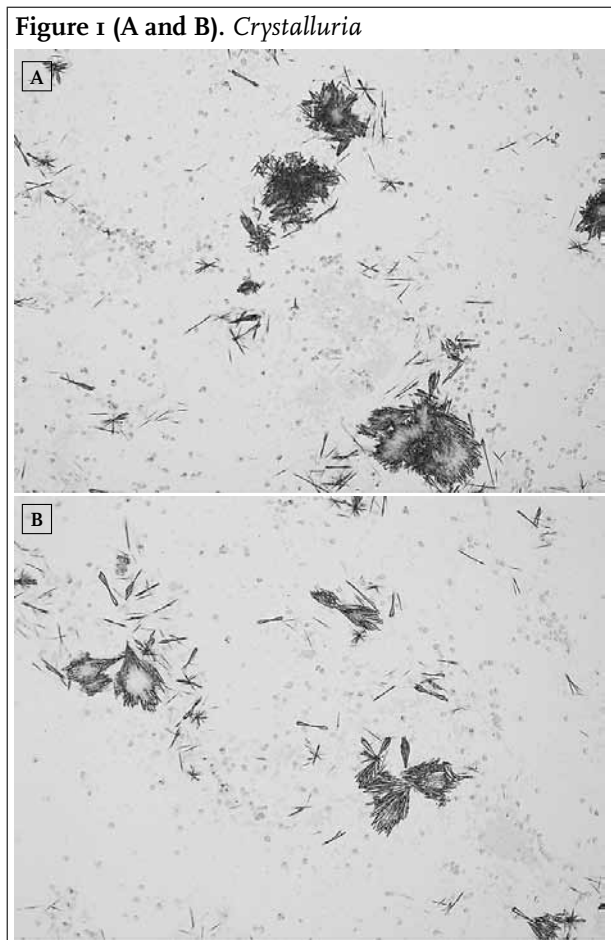
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CASE REPORT

A 68-year-old male was admitted to the hospital with a community-acquired pneumonia. He had a previous history of Parkinson's disease and benign prostatic hyperplasia; his medication consisted of levodopa/carbidopa (8 x 100/25 mg/day) and tamsulosin (0.4 mg/day). At admission, he had a normal renal function (GFR >90 ml/min) and a normal urine sample with a pH of 6. Treatment with intravenous amoxicillin/clavulanic acid (4 x 1000/200 mg/day) was started. During treatment the patient developed macroscopic haematuria. Repeated urine examination, three days after admission, showed the presence of erythrocytes, some leucocytes, a pH of 6 and multiple crystals (*figures 1A and B*) with a negative urine culture.

WHAT IS YOUR DIAGNOSIS?

See page 87 for the answer to the photo quiz.



DIAGNOSIS

The crystals were different from the crystals commonly seen, such as uric acid and calcium oxalate. The crystals appeared as needles, 'shocks of wheat', 'broom bush-like' and one sea urchin-shaped crystal. These atypical shaped crystals can be seen in patients using amoxicillin or ampicillin.¹ After replacing amoxicillin/ clavulanic acid by cefuroxim, crystals were no longer present in the urine sample from five days later, nor were erythrocytes and leucocytes present. The renal function remained normal (GFR >90 ml/min) during treatment with amoxicillin/ clavulanic acid.

Several drugs can cause transient crystalluria, including sulfadiazine, amoxicillin and ciproxin. Risk factors are drug overdose, dehydration, hypoalbuminaemia (which increases the fraction of unbound drug), and low (<4) or high (>7) urine pH, due to U-shaped pH solubility curves.^{1,2} Amoxicillin is excreted by the kidneys, 90% by the proximal tubules and 10% by glomerular filtration,² and can cause reversible asymptomatic crystalluria without renal damage, crystalluria with macroscopic haematuria or crystalluria with acute renal failure.¹ It is hypothesised that haematuria and renal failure are due to tubular damage and medullary congestion caused by intratubular precipitation of crystals; however, this has never been confirmed with renal biopsy.¹ After discontinuation, crystalluria usually disappears within 24 hours, haematuria within three days and acute renal failure in 3 to 17 days.²

Amoxicillin crystalluria was first described in 1985 in a 26-year-old healthy volunteer, who received an overdose of amoxicillin to investigate renal excretion. Three hours after termination of the infusion, crystals could no longer be found in the sediment. The crystalluria in this volunteer was probably due to the urinary concentration exceeding the urinary solubility of the drug in combination with a low urinary pH of 5.²

Recently, it was shown that crystalluria was present in 8.2% of almost 10,000 regular urine samples. In 8.1% of these samples 'typical' crystals were identified, mainly calcium oxalate and uric acid. Three out of 14 'atypical' crystals were due to use of a drug, one due to amoxicillin.³ In conclusion, our patient experienced reversible amoxicillin crystalluria with macroscopic haematuria without acute renal failure, possibly due to a relatively low urine pH, mild dehydration and urine retention due to benign prostatic hyperplasia. Crystalluria is a rare adverse event associated with use of amoxicillin.

REFERENCES

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3. Verdesca S, Fogazzi GB, Garigali G, Messa P, Daudon M. Crystalluria: prevalence, different types of crystals and the role of infrared spectroscopy. *Clin Chem Lab Med.* 2011 Mar;49(3):515-20.