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We report a case of acute kidney injury (AKI) induced by amoxycillin crystalluria suggested by massive amounts of urinary crystals of unusual morphology. This hypothesis was further reinforced by a particular solubility pattern when the urine sample was exposed to various temperatures, alkali, acids and alcohol. We therefore suspended amoxycillin, which produced a rapid and complete recovery of kidney function. Infrared spectroscopy later confirmed the amoxycillin composition of the crystals. Since infrared spectroscopy is not easily available, we propose that these solubility tests of urinary crystals be used as a first-step investigation when amoxycillin crystalluria is suspected.

Reference

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EXCEPTIONAL CASE

The Friday evening case of acute kidney injury: a crystal dilemma

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Abstract

We report a case of acute kidney injury (AKI) induced by amoxycillin crystalluria suggested by massive amounts of urinary crystals of unusual morphology. This hypothesis was further reinforced by a particular solubility pattern when the urine sample was exposed to various temperatures, alkali, acids and alcohol. We therefore suspended amoxycillin, which produced a rapid and complete recovery of kidney function. Infrared spectroscopy later confirmed the amoxycillin composition of the crystals. Since infrared spectroscopy is not easily available, we propose that these solubility tests of urinary crystals be used as a first-step investigation when amoxycillin crystalluria is suspected.

Key words: acute kidney injury, amoxycillin, crystalluria, solubility tests, urinary sediment

Background

Acute kidney injury (AKI) is a serious complication occurring in 21% of critically ill hospitalized patients that is associated with increased morbidity, mortality and costs [1]. Among causes of hospital-acquired AKI, amoxycillin may be rarely implicated through massive intrarenal or post-renal precipitation of crystals made up of the drug itself [2].

We report the case of a patient with AKI induced by amoxycillin crystalluria in which the diagnosis was suggested by a specific pattern of crystal solubility and was then confirmed by infrared spectroscopy.

Case report

On 7 November 2016, an 80-year-old obese and hypertensive woman was admitted for severe back pain with fever. Her past clinical history was unremarkable. At admission, serum creatinine was 79 µmol/L (0.9 mg/dL) with a normal urine dipstick. On 9 November, intravenous amoxycillin 2.2 g four times daily was started following the diagnosis of pyogenic spondylodiscitis caused by Parvimonas micra. Other medications included ibuprofen 600 mg twice daily for back pain and olmesartan 20 mg daily for hypertension. The next day, serum creatinine rose to 122 µmol/L (1.38 mg/dL). Ibuprofen and olmesartan were...
Calcium oxalate is unk. Uric acid is sol. Crystals can be heat treated at various temperatures (27, 30 and 60°C) under polarized light (Supplementary data, Figure S1). Since the morphology of the crystals was unusual, the urine sample was exposed to the following physical and chemical conditions: heat (27, 30 and 60°C), alkali (NaOH 0.1 M), acids (HCl 25% and CH₃COOH 1.0 mmol/L) and alcohol (70%).

<table>
<thead>
<tr>
<th>Crystals</th>
<th>Heat</th>
<th>HCl 25% (pH 3)</th>
<th>CH₃COOH 1.0 mmol/L (pH 5.5)</th>
<th>NaOH 0.1 M (pH 8)</th>
<th>Alcohol 70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid</td>
<td>S</td>
<td>I</td>
<td>I</td>
<td>S</td>
<td>I</td>
</tr>
<tr>
<td>Calcium oxalate²</td>
<td>unk</td>
<td>S</td>
<td>I</td>
<td>S</td>
<td>unk</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>I</td>
<td>S</td>
<td>S</td>
<td>I</td>
<td>unk</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>S</td>
</tr>
<tr>
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<td>unk</td>
<td>I</td>
<td>S</td>
<td>S</td>
<td>I</td>
</tr>
<tr>
<td>Leucine</td>
<td>unk</td>
<td>I</td>
<td>I/S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>S</td>
<td>S</td>
<td>I</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Ammonium</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>unk</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>I</td>
<td>S</td>
<td>I</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>

Similar to calcium oxalate, cystine, tyrosine and ammonium crystals, urinary crystals from our patient were found to be soluble in highly acidic (pH 3.0) and alkaline (pH 8.0) solutions. In contrast, they were insoluble when exposed to different temperatures, pH 5.5 and alcohol 70%.

²Please note that calcium oxalate and amoxycillin crystals show the same solubility behaviour when exposed to alkali (NaOH 0.1 M) and different acids (HCl 25% and CH₃COOH 1.0 mmol/L), but they are easily distinguishable in morphology.

I, insoluble; S, soluble; unk, unknown.

Amoxycillin crystalluria is rare. Single cases have been reported in paediatric patients after accidental ingestion and/or overdose of the drug and in adults treated with high doses of amoxycillin. Crystalluria may be isolated or associated with microscopic and/or gross haematuria and leucocyturia, with or without oliguric AKI. This may be due to urinary tract obstruction caused by massive crystal precipitation in the renal pelvis or in the renal tubules, with subsequent tubulopathy and medullary congestion. However, this hypothesis has not been confirmed by renal biopsy [2].

Approximately 80% of amoxycillin is excreted unchanged in the urine and, similar to other antimicrobial agents, may cause crystalluria, especially when the drug is overdosed, in hypoaalbuminaemic states or in mid-range urinary pH (between 4.0 and 7.0) [2].

Amoxycillin crystals differ in morphology from other urinary crystals. In this context, the exposure of urine samples to a variety of standardized physical and chemical conditions is proposed as a simple and inexpensive test to reinforce the suspicion of amoxycillin crystalluria. In our case, this test led to immediate discontinuation of the drug, a difficult decision to make in this critical situation, which in turn induced a rapid recovery from AKI. However, the definitive confirmation of this diagnosis may only be provided by infrared spectroscopy [2], a technique that is not easily and promptly available.

In conclusion, we propose that the suspicion of amoxycillin crystalluria should prompt the use of these urinary solubility tests, which may prove to be instrumental for bedside clinical decisions, at least until infrared spectroscopy is performed.

**Discussion**

Amoxycillin crystalluria is rare. Single cases have been reported in paediatric patients after accidental ingestion and/or overdose.

**Supplementary data**

Supplementary data are available online at http://ckj.oxfordjournals.org.

**Acknowledgements**

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**Conflict of interest statement**

None declared.
References


