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How to cite

GUZZO, Gabriella et al. The Friday evening case of acute kidney injury: a crystal dilemma. In: Clinical Kidney Journal, 2018, vol. 11, n° 4, p. 450–452. doi: 10.1093/ckj/sfx114

This publication URL: https://archive-ouverte.unige.ch/unige:111679
Publication DOI: 10.1093/ckj/sfx114

Clinical Kidney Journal, 2018, vol. 11, no. 4, 450–452

doi: 10.1093/ckj/sfx114
Advance Access Publication Date: 18 October 2017
Exceptional Case

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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

Received: July 26, 2017. **Editorial decision:** August 28, 2017

Table 1. Behaviour of amoxycillin crystals compared with other crystals found in urine when exposed to different physical and chemical conditions: heat (27, 30 and 60°C), alkali (NaOH 0.1 M), acids (HCl 25% and CH_3COOH 1.0 mmol/L) and alcohol (70%)

Crystals	Heat	HCl 25% (pH 3)	CH_3COOH 1.0 mmol/l (pH 5.5)	NaOH 0.1 M (pH 8)	Alcohol 70%
Uric acid	S	I	I	S	I
Calcium oxalate[a]	unk	S	I	S	unk
Calcium phosphate	I	S	S	I	unk
Cholesterol	unk	unk	unk	unk	S
Cystine	unk	S	I	S	I
Leucine	unk	I	I/S	S	S
Tyrosine	S	S	I	S	I
Ammonium	S	S	S	S	unk
Amoxycillin	I	S	I	S	I

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%.

[a]Please 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 CH_3COOH 1.0 mmol/L), but they are easily distinguishable in morphology.

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

withdrawn and the patient was hydrated with intravenous sodium chloride. However, renal function continued to deteriorate rapidly, with serum creatinine peaking at 450 μmol/L (5.09 mg/dL) in association with oliguria. This led to the so-called Friday evening call to the nephrologist. We found a normotensive and mildly dehydrated patient with normal kidneys at bedside abdominal echography. The fractional excretion of sodium of 0.6% indicated pre-renal AKI. Urinary dipstick showed a pH 5.0, relative density 1.030, albumin 100 mg/dL, haemoglobin 250 erythrocytes/μL and leucocyte esterase 500 leucocytes/μL. The urine sediment, examined by both bright field and phase contrast microscopy at low (100×) and high (400×) magnifications, showed severe crystalluria [>30 crytals/high-power field (HPF)] associated with mild leucocyturia (~8 white blood cells/HPF) and moderate isomorphic haematuria (~20 red blood cells/HPF). Crystals appeared as thin and colourless needles and rods, either in individual structures or in clusters, and strongly birefringent 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 [3]: various temperatures (27, 30 and 60°C), alkali (NaOH 0.1 M), acids (HCl 25% and CH_3COOH 1.0 mmol/L) and alcohol 70%. Crystals showed a peculiar solubility pattern different from other known urinary crystals (Table 1).

Therefore, considering the short time interval between the first administration of amoxycillin and the onset of AKI, we hypothesized that crystals could be due to intrarenal amoxycillin precipitation [4]. This drug was immediately suspended and replaced by clindamycin, 600 mg three times daily. In addition, 1.4% intravenous sodium bicarbonate was given to increase the crystals' solubility through urine alkalinization and reverse hypovolaemia. This led to a rapid induction of diuresis and the disappearance of crystalluria within 24 h. Three days later, a full recovery of renal function was observed. Spondylodiscitis was successfully treated with clindamycin. Infrared spectroscopy of crystals, performed on 15 November, showed a wave spectrum exactly matching the amoxycillin spectrum reported by others [5].

Discussion

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 hypoalbuminaemic 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.

Supplementary data

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

Acknowledgements

We would like to thank Valia Humbert-Delaloye, PhD from the Department of Pharmacy, Central Institute of Hospitals, Hospital of Wallis, for providing us the infrared spectroscopy urinary crystals analysis.

Conflict of interest statement

None declared.

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