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► **To cite this version:**

Camille Saint-Jacques, Audrey Uzan, Elise Marechal, Vincent Frochot, Jean-Philippe Haymann, et al.. The Case | An 80-year-old man with obstructive uropathy. *Kidney International*, 2022, 102 (5), pp.1197-1198. 10.1016/j.kint.2022.03.018 . hal-04184036

**HAL Id: hal-04184036**

**<https://hal.sorbonne-universite.fr/hal-04184036>**

Submitted on 21 Aug 2023

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The Case : An 80-year-old man with obstructive uropathy

Camille Saint-Jacques,<sup>1</sup> Audrey Uzan,<sup>2</sup> Elise Marechal,<sup>1</sup> Vincent Frochot,<sup>1</sup> Jean-Philippe Haymann,<sup>1,3</sup> Olivier Traxer,<sup>2,3</sup> Michel Daudon,<sup>1</sup> Emmanuel Letavernier,<sup>1,3</sup>

<sup>1</sup> Assistance Publique des Hôpitaux de Paris, Service des Explorations Fonctionnelles Multidisciplinaires, Hôpital Tenon, Paris, France

<sup>2</sup> Assistance Publique des Hôpitaux de Paris, Service d'Urologie, Hôpital Tenon, Paris, France

<sup>3</sup> Sorbonne Université, Institut National de la Santé et de la Recherche Médicale Unité Mixte de Recherche 1155- UMR S 1155

Correspondence: Emmanuel Letavernier, Service des Explorations Fonctionnelles Multidisciplinaires, Hôpital TENON, 4 rue de la Chine, 75020 Paris, France. E-mail : [emmanuel.letavernier@aphp.fr](mailto:emmanuel.letavernier@aphp.fr)

The authors declare no conflict of interest relative to this case

Key words: acute renal failure, kidney stones, 1-methyluric acid, coffee

Word Count: The case: 221; The diagnosis: 368

## The case

An 80-years old man was hospitalized for an acute renal failure due to bilateral obstructive urolithiasis, with a creatinine serum level at 430  $\mu\text{mol/L}$ . His past medical history revealed a renal colic 20 years ago, poorly controlled hypertension, obesity, type 2 diabetes treated with insulin, ischemic heart disease, ischemic stroke, and a chronic kidney disease from unknown origin with a baseline serum creatinine value around 170  $\mu\text{mol/L}$ . The abdominal computed tomography (CT)-scan showed a bilateral ureteral obstruction caused by multiple stones. A stone measuring 17 mm was located at the right kidney pyelo-ureteral junction and a stone measuring 4 mm was located at the left uretero-vesical junction. Several bilateral small stones were also observed (Figure 1). The density of the largest stone was low, 250 Hounsfield Units (HU). After undergoing bilateral ureteral stent, the serum creatinine decreased rapidly to 200  $\mu\text{mol/L}$ , and the patient underwent bilateral reno-ureteroscopies allowing ureteral stones fragmentation. Other urine and blood tests revealed a very low fasting urine pH at 4.7, increased serum uric acid levels at 511  $\mu\text{mol/L}$ , and a relatively low uric acid excretion at 1 mmol/l in a morning urine collection. He had a mild proteinuria (0.38 g/day). The morphological analysis of kidney stone fragments revealed an unusual aspect with a rusty brown surface and a heterogeneous section with a brown to salmon pink color (Figure 2). Fourier transformed infrared spectroscopic analyses revealed 1-methyluric acid as the main component of the kidney stones.

What is your diagnosis?

Obstructive uropathy due to bilateral 1-methyluric acid (1-MUA) kidney stones from heavy caffeine intake

1-MUA is the main caffeine metabolite identified in urine. A report previously described 1-MUA kidney stones mixed with calcium oxalate in an individual affected by gouty attacks and drinking at least 8 cups of coffee per day.<sup>1</sup> Moreover, 20 stones containing 1-MUA were analyzed in Necker and Tenon Hospital laboratories in Paris during the past decades.<sup>2</sup> Most of these stones came from avid consumers of coffee affected by end-stage renal failure and treated with aluminum hydroxide,

suggesting that this compound may interfere with caffeine metabolism. More recently, we reported that 1-MUA may be causative for acute crystalline nephropathy.<sup>3</sup> Of note the patient was affected by type 2 diabetes, a condition leading to a low urine pH due to a decrease in ammoniogenesis, and causative for uric acid stones formation. Considering the structure of 1-MUA, its expected pKa should be similar to the pKa of uric acid (pKa1: 5.4), 1-MUA is therefore prone to crystallize when urine pH is low. One may hypothesize that the formation of 1-MUA stones may have resulted from the combination of high caffeine intakes and low urine pH, both increasing 1-MUA crystallization. Another common feature of uric acid and 1-MUA kidney stones is their low density on CTscans, as evidenced in this case (250 HU). To prevent recurrence, the patient decreased coffee intakes (1-2 cups/day), increased water intakes including alkaline water (Vichy St Yorre® 1 liter/day). He remained stone-free 8 months after reno-ureteroscopies but chronic kidney disease (CKD) remained stable with a serum creatinine around 170  $\mu\text{mol/L}$  (GFR measured by DTPA-Techetium clearance: 31 ml/min/1.73 m<sup>2</sup>). CKD was likely due to nephroangiosclerosis and may have been worsened by obstructive nephropathy and/or 1-MUA intratubular precipitation. This case illustrates that 1-MUA urolithiasis may present as uric acid stones, and may also lead to acute obstructive renal failure, in addition to crystalline nephropathy. This observation emphasizes the need for stone analysis including FTIR or other spectroscopic methods.

#### References

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#### Figures

Figure legends:

Figure 1: CT-scan performed during the acute obstructive episode (bone window) showing low-density bilateral kidney stones (arrows).

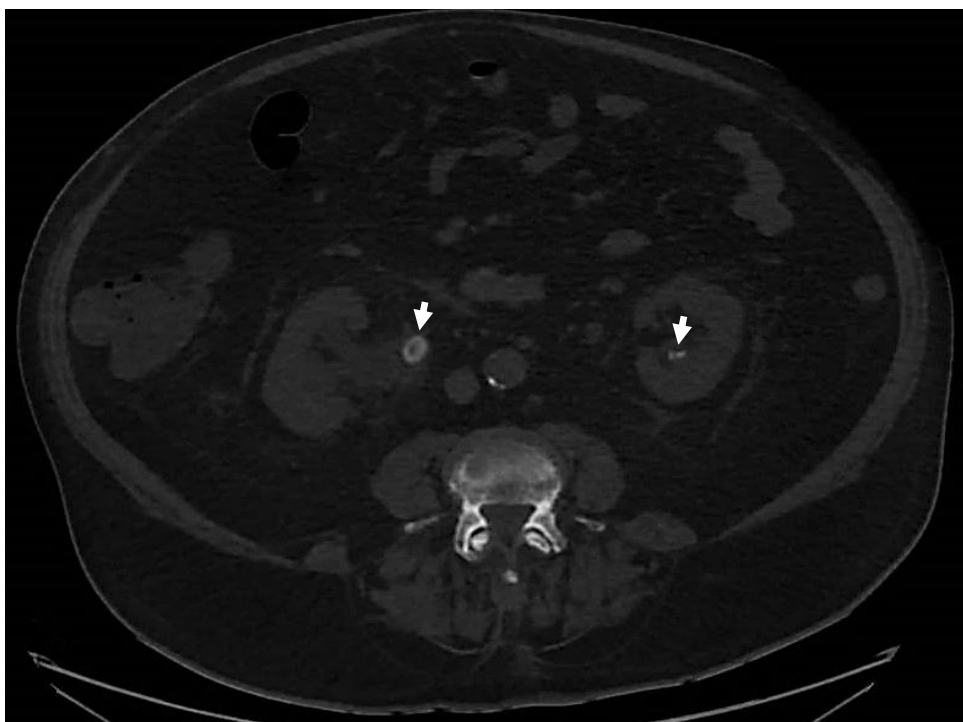


Figure 2: stone fragment removed during reno-ureteroscopy



