Acute bilateral ureteral obstruction secondary to guaifenesin toxicity

Patrick A. Cockerill, MD, Mitra R. de Cógáin, MD, Amy E. Krambeck, MD
Department of Urology, Mayo Clinic College of Medicine, Rochester, Minnesota, USA

COCKERILL PA, DE COGAIN MR, KRAMBECK AE. Acute bilateral ureteral obstruction secondary to guaifenesin toxicity. *Can J Urol* 2013;20(5):6971-6973.

Several medications or their metabolites have been associated with urolithiasis, although overall they remain an infrequent cause of urolithiasis. Guaifenesin stones were originally reported as complexed with ephedrine, and subsequent reports have demonstrated pure guaifenesin stones, occurring after long term abuse. We report a case of a 23-year-old male who ingested a large, one time dose of guaifenesin, resulting in acute bilateral ureteral obstruction, which, to our knowledge, is the first such reported case in the literature.

Key Words: urolithiasis, medication, ureteral obstruction

Introduction

The prevalence of urolithiasis is approximately 8.8% in the United States.[1] However, calculi associated with medications and their metabolites are an infrequent cause of urinary stones. Medications whose metabolites have been associated with urolithiasis include ciprofloxacin, sulfa medications, triamterene, indinavir, guaifenesin and ephedrine.[2] The majority of urolithiasis cases reported in association with medications are discrete calculi which form after long term use, abuse, or overdose of the drugs mentioned. In some instances the medication induced stones require surgical extraction due to an inability to pass through the collecting system. We report a case of acute ureteral obstruction caused by an acute overdose of guaifenesin, which, to our knowledge, is the first such case reported in the literature.

Case report

A 23-year-old man with no past medical history presented to the emergency department with the acute onset of bilateral flank pain radiating to the scrotum, with associated hematuria and dysuria. His social history was remarkable for alcohol dependence and occasional cannabis use. In an attempt to "get high" but avoid alcohol secondary to his history of dependence, he reportedly ingested 10 tablets of guaifenesin 600 mg with dextromethorphan 30 mg (Mucinex DM).

Accepted for publication May 2013

Address correspondence to Dr. Amy Krambeck, Department of Urology, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905 USA

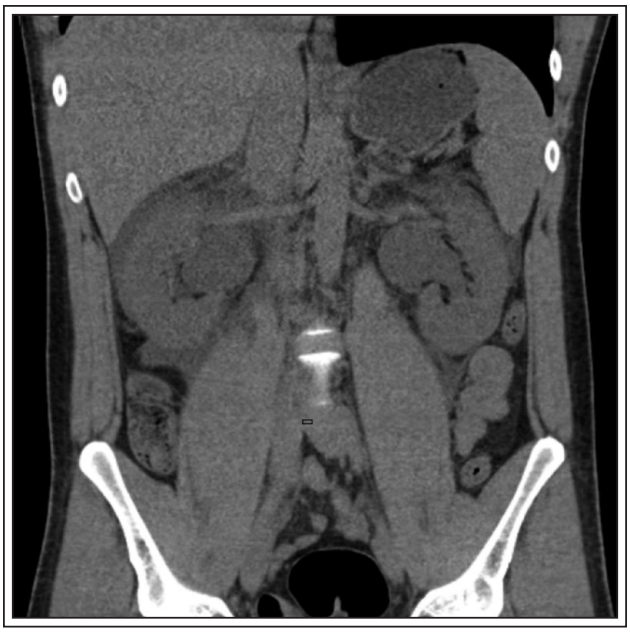

Figure 1. Coronal section of the abdomen, showing bilateral hydronephrosis.

Upon arrival to the emergency department, the patient was hypertensive but otherwise stable, with a leukocytosis of 21,000 and a creatinine of 2.5. Computed tomography of the abdomen and pelvis was significant for bilateral hydroureteronephrosis with associated perinephric edema, Figure 1. Along 3 cm segments of the ureters bilaterally, just proximal to the ureterovesical junctions, hyperdense material was noted, without discrete urolithiasis, Figures 2 and 3. The patient was taken emergently to the operating room, for cystoscopic indwelling double-J ureteral stent placement. Gross inspection of the bladder demonstrated flocculent, whitish debris protruding from the ureteral orifices bilaterally, and at the dependent portion of the bladder.

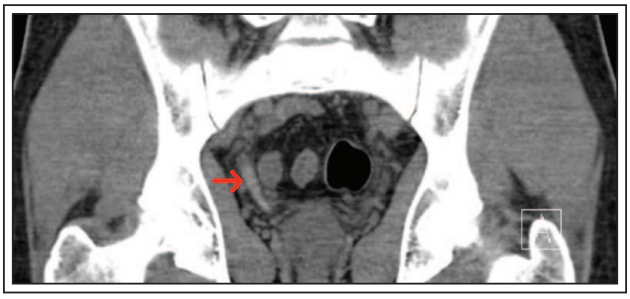

Figure 2. Coronal section through the pelvis, showing hyperdense material in the right distal ureter (arrow) without a discrete calculus.

Specimens from the bladder were obtained with forceps, and specimens from both ureters were aspirated with an open ended ureteral catheter prior to stent placement. All specimens were sent for Fourier transform infrared spectroscopy (FTIR) which demonstrated guaifenesin metabolites. Six weeks later, the patient underwent uncomplicated bilateral stent removal. Follow up intravenous pyelogram demonstrated no evidence of residual material or obstruction, and serum creatinine was 1.2 mg/dL.

Discussion

Medication induced urolithiasis is rare and accounts for 1%-2% of all renal calculi.[3] Multiple different medications have been associated with urolithiasis, including guaifenesin, but acute bilateral ureteral obstruction has not been previously reported. The combination of guaifenesin and ephedrine urolithiasis was first reported by Assimos and colleagues.[4] Their group demonstrated guaifenesin metabolites from seven patients by infrared spectroscopy or x-ray crystallography. Analysis of the stone material revealed that the majority (70%) was composed of guaifenesin metabolites, with lesser amounts of ephedrine (5%) and unspecified other substances (25%). The patients in their study ingested 10 to 20 grams of guaifenesin per day (between 50 and 100 tablets of guaifenesin 200 mg), although the length of time the patients were abusing the drug and overall exposure time is not reported.

Pickens and colleagues originally described the identification of guaifenesin stones.[5] They analyzed 30 stones from 24 patients with infrared spectroscopy and mass spectroscopy, and identified 27 stones that were composed of 100% beta-(2-methoxyphenoxy)-lactic acid, a metabolite of guaifenesin, with the remaining three stones composed of lesser amounts of the substance

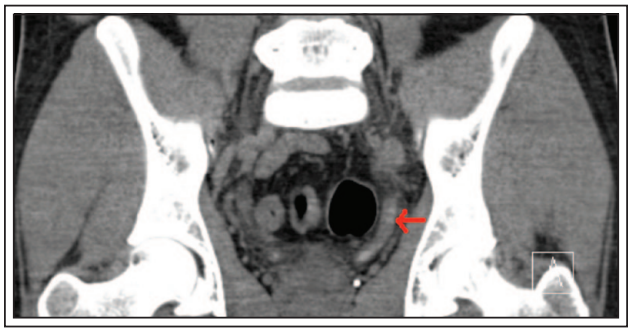

Figure 3. Coronal section through the pelvis, showing hyperdense material in the left distal ureter (arrow) without a discrete calculus.

complexed with calcium phosphate or calcium oxalate. The groups reported an overall guaifenesin stone incidence of 0.05% during the study period.

Guaifenesin stones are radiolucent on standard radiography and radiodense on computed tomography. Treatment of guaifenesin stones has been undertaken by standard ureteroscopic approaches, although spontaneous dissolution with increased hydration has been reported.[6]

Our patient presented uniquely different from previous reports, as sludging of guaifenesin in the distal ureters caused acute bilateral ureteral obstruction, and he had no evidence of a true ureteral calculus. Assimos' original description was in patients chronically taking 10 or more grams of guaifenesin per day (fifty 200 mg guaifenesin tablets), causing discrete urolithiasis. In contrast, our patient reportedly took a one time dose of 6 grams of guaifenesin, resulting in acute bilateral ureteral obstruction. This emphasizes that high doses of guaifenesin can not only result in the formation of discrete urolithiasis, but in acute ureteral obstruction. □

References

1. Scales CD Jr, Smith AC, Hanley JM, Saigal CS; Urologic Diseases in America Project. Prevalence of kidney stones in the United States. *Eur Urol* 2012;62(1):160-165.
2. Matlaga BR, Shah OD, Assimos DG. Drug-induced urinary calculi. *Rev Urol* 2003;5(4):227-231.
3. Daudon M, Jungers P. Drug induced renal calculi: epidemiology, prevention, and management. *Drugs* 2004;64(3):245-275.
4. Assimos DG, Langenstroer P, Leinbach RF, Mandel NS, Stern JM, Holmes RP. Guaifenesin- and ephedrine-induced stones. *J Endourol* 1999;13(9):665-667.
5. Pickens CL, Milliron AR, Fussner AL et al. Abuse of guaifenesin-containing medications generates an excess of a carboxylate salt of beta-(2-methoxyphenoxy)-lactic acid, a guaifenesin metabolite, and results in urolithiasis. *Urology* 1999;54(1):23-27.
6. Nguyen TT, Fallon B, Winfield HN. Spontaneous dissolution of a guaifenesin stone. *Can J Urol* 2005;12(4):2769-2771.
7. Whelan C, Schwartz B. Bilateral guaifenesin ureteral calculi. *Urology* 2004;63(1):175-176.