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Bilateral nephrolithiasis following ingestion of guaifenesin and dextromethorphan

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ABSTRACT

Both guaifenesin and dextromethorphan are routinely available nonprescription medications that are also common drugs of abuse amongst young adults. We describe a presentation of guaifenesin and dextromethorphan misuse resulting in acute renal failure due to bilateral nephrolithiasis. The patient underwent placement of bilateral ureteral stents but again formed small renal stones bilaterally. While most renal calculi are not drug-induced, this case highlights the potential for nephrolithiasis after guaifenesin and dextromethorphan ingestion. It suggests that in this combination ingestion multiple mechanisms lead to a prolonged period of nephrolith formation.

1. Introduction

According to the National Survey on Drug Use and Health, 389,000 young adults misused cough and cold medicines over a year.[1] One such medicine, Mucinex DM, contains the active components dextromethorphan and guaifenesin. Using large amounts of cough/cold medicines to obtain psychoactive effects can result in a toxidrome of delirium, paranoia, and hallucinations.[2] A less common side effect of guaifenesin abuse is the formation of drug-induced ureteral stones.[3–5] Drug-induced stones represent a small percentage, approximately 1–2%, of all ureteral stones.[3–5] To our knowledge there is only one previous case report documenting drug-induced nephrolithiasis in the setting of guaifenesin/dextromethorphan ingestion.[3] Here we describe a presentation of bilateral nephrolithiasis and acute renal failure following ingestion of guaifenesin/dextromethorphan. This case suggests an indication for closer monitoring of patients with guaifenesin/dextromethorphan-induced calculi due to the potential for prolonged precipitation of drug metabolites and stone formation.

2. Case presentation

A 19-year-old male was found after reportedly ingesting a full box of Mucinex DM. He was agitated in the Emergency Department (ED), requiring multiple doses of sedative medication and intubation. His initial laboratory findings were notable for a creatinine of 1.36 and microscopic hematuria.

He was admitted to the intensive care unit. Throughout the day on hospital day zero he became oliguric. Etiology including hypovolemia and acute tubular necrosis were considered. The patient's oliguria progressed to anuria despite receiving additional intravenous fluids increasing suspicion for a post-renal source. Foley was flushed and bladder ultrasound revealed a decompressed bladder with minimal urine. His acute kidney injury worsened with a creatinine elevation to 3.86 15 h after presentation. Urology was consulted, and CT scan demonstrated nonobstructing stones in the inferior poles of both kidneys [Fig. 1]. Urine mass spectrometry resulted positive for dextromethorphan, levorphanol, a dextromethorphan metabolite, and guaifenesin [Fig. 2].

On hospital day one he underwent cystourethroscopy with placement of bilateral ureteral stents. No stones were visible on fluoroscopy scout images. Intraoperatively he was noted to have severe snowy calcification debris in the bladder, bilateral ureteral orifices, and ureters. Over the subsequent 24 hours he had 6 L of urine output. His creatine normalized, and he was discharged.

Patient presented to the ED three days later with flank pain, leukocytosis to 15.5, and hematuria. He was evaluated by urology and underwent stent exchange. He was noted to have renal stones bilaterally. Calculi analysis noted calculi were composed of calcium oxalate and calcium phosphate. Narrative described suspected guaifenesin stones

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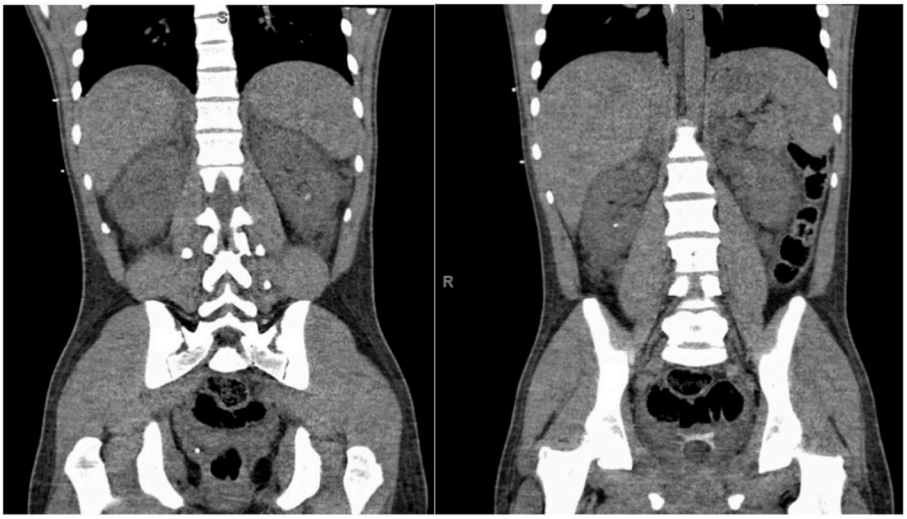

Fig. 1. Computed tomography scan of the abdomen and pelvis without IV contrast demonstrating hyperdense material in the inferior poles of the right and left kidneys and calcified phleboliths in the right and left hemi pelvises.

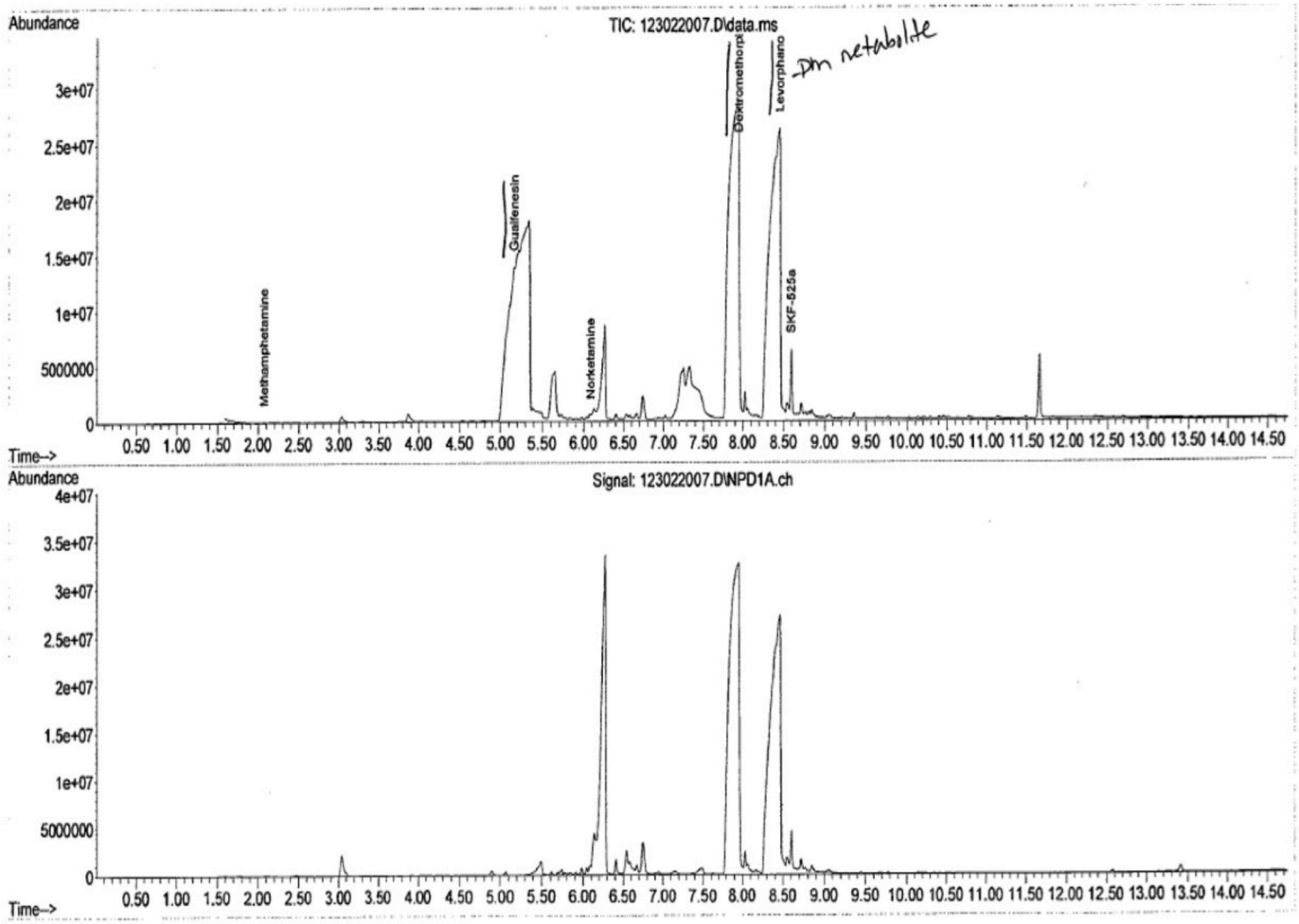

Fig. 2. Urine mass spectrometry with presences of dextromethorphan, dextromethorphan metabolite levorphanol, and guaifenesin.

which may need additional testing. Composition by Fourier Transform Infrared Spectroscopy (FTIR) analysis was unable to be obtained. The patient was scheduled for stent removal in four weeks but was lost to follow up.

3. Discussion

Dextromethorphan and guaifenesin are common components of cough and cold medicines. The development of renal stones following consumption of large amounts of guaifenesin is rare but was first

reported in 1999.[4] Matgala et al. described two primary mechanisms by which medications can induce urinary stone disease: urinary supersaturation and crystallization of a drug or one of its metabolites or a drug creating physiologic changes that facilitate the formation of metabolic stones.[5] For preparations of guaifenesin, the former mechanism is most likely.[5] Assimos and colleagues analyzed stones from seven patients who consumed large amounts of guaifenesin and ephedrine.[4] They utilized FTIR and high-resolution X-ray crystallographic powder diffraction to demonstrate that 70% of stone material was a guaifenesin metabolite.[4]

We have encountered only one prior case report which discusses nephrolith formation after consumption of guaifenesin and dextromethorphan.[3] In Small and Sandefur's patient presentation, ureteral precipitate rather than a well-formed stone was found on ureteroscopy.[3] They concluded that precipitation of drug metabolites was responsible for acute ureteral obstruction.[3] This was supported by debris analyzed by FTIR containing predominantly guaifenesin metabolites.[3] The patient in Small and Sandefur's case underwent bilateral stent placement with subsequent uncomplicated removal of stents at a four week follow up with urology.[3]

Like Small and Sandefur's report, our patient was found to have bilateral ureteral obstruction after ingestion of a preparation of guaifenesin/dextromethorphan. During cystourethroscopy he did not have discrete stone formation but had snowy calcification debris in the bladder, ureteral orifices, and ureters indicative of precipitation of drug metabolites. Interestingly, calculi analysis noted calculi were composed of calcium oxalate and calcium phosphate. Narrative described suspected guaifenesin stones, but definitive composition by FTIR analysis was unable to be obtained. We suggest that the severity of this patient's presentation was due to a combination of the two proposed mechanisms of drug-induced stone formation. While precipitation of guaifenesin metabolites likely occurred, it is also possible a guaifenesin/dextromethorphan combination potentiated formation of metabolic stones. In contrast to Small and Sandefur, our patient re-presented to the ED and 12 days after his initial procedure required exchange of bilateral stents. At that time, he was noted to have renal stones bilaterally. It is possible the combination of dextromethorphan with guaifenesin prolonged the duration of precipitation of guaifenesin/dextromethorphan metabolites.

In patients with acute renal failure following ingestion of guaifenesin/dextromethorphan we encourage providers to consider bilateral nephrolithiasis. If bilateral nephrolithiasis is encountered, we suggest closer monitoring with strict intake and output documentation during hospitalization due to the potential of ongoing stone formation up to 12 days after initial presentation. Additionally, information regarding symptoms of ureteral obstruction and return precautions should be communicated with patients, and we would advocate for closer follow up with urology for stent evaluation.

4. Conclusion

This report draws awareness to the clinical finding of drug induced nephrolithiasis. One prior case of bilateral ureteral obstruction and acute post obstructive renal failure in the setting of guaifenesin/dextromethorphan overdose has been reported. We acknowledge our study is limited by the inability to analyze stones with FTIR. However, this case suggests that in guaifenesin/dextromethorphan ingestion both mechanisms of drug metabolite precipitation and physiologic changes that facilitate the formation of metabolic stones are involved in acute renal failure. Additionally, this case provides evidence that patients with development of bilateral nephrolithiasis after guaifenesin/dextromethorphan ingestion require closer monitoring during hospitalization and closer follow up outpatient due to the risk of ongoing stone formation.

Consent

Informed consent was taken from the patient for publication of this case report and the associated images.

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Declaration of competing interest

None.

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