UROLITHIASIS ASSOCIATED WITH TOPIRAMATE

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ABSTRACT

Objective: Topiramate is a sulfamate-substituted monosaccharide anticonvulsant used as adjunctive therapy for intractable refractory seizures. It is report a case of topiramate-induced urolithiasis.

Case Report: A 35-year-old man presented with acute, right-sided, colicky flank pain. He denied hematuria or dysuria. He was in use of phenytoin, risperidone, phenobarbital, and topiramate. The total daily dose of topiramate was 375 mg. A CT scan showed a 7 x 1 mm curvilinear density at the right ureterovesical junction with proximal hydroureteronephrosis. He was managed with rigid ureteroscopic stone extraction and the calculus metabolic analysis revealed the stone was composed of carbonate apatite (70%), calcium oxalate dihydrate (20%), and calcium oxalate monohydrate (10%).

Comments: The present case typifies many features of topiramate-induced urolithiasis. Those who care for patients with urinary stone disease should be aware of this association.

Key words: urolithiasis; acids; metabolism; anticonvulsants; adverse effects

INTRODUCTION

Topiramate is a sulfamate-substituted monosaccharide anticonvulsant used as adjunctive therapy for intractable refractory seizures. We report a case of topiramate induced urolithiasis.

CASE REPORT

A 35-year-old man presented with acute, right-sided, colicky flank pain. He denied hematuria or dysuria. He denied any prior history of stones, was not on a high protein or low carbohydrate (ketogenic) diet, and his family history was noncontributory. Following viral encephalitis at the age of 18, he developed a seizure disorder that was being treated with phenytoin, risperidone, phenobarbital, and topiramate. The total daily dose of topiramate was 375 mg.

He appeared well and had normal vital signs. There was no tenderness to palpation of the abdomen or costovertebral angles. His white blood cell count was 12,100/mL and serum creatinine was 1.2 mg/dL. Urinalysis revealed a pH of 7.5, without hematuria or evidence of infection. A CT scan showed a 7 x 1 mm curvilinear density at the right ureterovesical junction with proximal hydroureteronephrosis (Figure-1).

He was managed initially with intravenous hydration and analgesics. His renal colic continued and the following morning the patient underwent cystoscopy, rigid ureteroscopy, and stone extraction. Small stone fragments were removed from the bladder and the right ureteral orifice without difficulty. A retrograde contrast study showed persistent distal ureteral obstruction, thus rigid ureteroscopy was performed. A tortuous and edematous distal ureter with a persistent stone fragment was encountered and
UROLITHIASIS ASSOCIATED WITH TOPIRAMATE

attempts at guide wire placement around the stone fragment were unsuccessful. The following day a percutaneous antegrade nephrostogram revealed mild hydronephrosis and narrowing at the right ureterovesical junction. A nephroureteral stent was placed. He was discharged the following day.

Metabolic analysis revealed the stone was composed of carbonate apatite (70%), calcium oxalate dihydrate (20%), and calcium oxalate monohydrate (10%).

COMMENTS

Clinical trials of topiramate reported a 1.5% incidence of urinary calculi, all occurring in males (1). Apatite, a rare stone associated with alkalosis, was the primary component in 5 of the 7 patients that had a stone analysis. Only 17% of the stone-forming patients elected to discontinue topiramate. Twelve patients underwent urine studies, all showing hypocitraturia, increased calcium phosphate saturation, and no effect on calcium excretion (2). Citrate levels below 100 mg/24 h have been observed in patients on the lowest doses of topiramate (100-300 mg/day). Additionally, in vitro studies of topiramate have demonstrated carbonic anhydrase inhibition (2). The metabolic and clinical effects are similar to acetazolamide, thus it is not surprising that these 2 medications have a similar incidence of urolithiasis (3). Our case typifies many features of topiramate-induced urolithiasis. Those who care for patients with urinary stone disease should be aware of this association.

REFERENCES


EDITORIAL COMMENT

In the current manuscript, the authors present a case report describing the formation of a carbonate apatite stone caused by an anti-convulsant medication, topiramate.

Previous studies have suggested that topiramate, in addition to a ketogenic diet, may be the cause of this drug induced calculus. It is currently well known that a ketogenic diet, usually one high in
animal protein and low in carbohydrates, is a significant risk factor for stones and may have contributed to the stone formation in this particular patient.

**References**


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