Case Study - Case Studies in Cystinuria

Article *in* Urologic nursing: official journal of the American Urological Association Allied · March 2017

DOI: 10.7257/1053-816X.2017.37.2.90

2 authors, including:

David S Goldfarb
NYHHS/NYU
305 PUBLICATIONS **9,842** CITATIONS

SEE PROFILE

HHS Public Access

Author manuscript

Urol Nurs. Author manuscript; available in PMC 2018 January 11.

Published in final edited form as:

Urol Nurs. 2017 ; 37(2): 90–93.

Case Studies in Cystinuria

David S. Goldfarb, MD and

Clinical Chief, Nephrology Division, New York University Langone Medical Center, and a Professor of Medicine and Physiology, New York University School of Medicine, New York, NY

Michael Grasso, MD

Professor and Vice Chairman, Department of Urology, New York Medical College, Valhalla, NY

Abstract

The diagnosis and treatment of patients with rare inherited metabolic disorders associated with recurrent and often obstructive kidney stones are important to the prevention of chronic kidney disease or end stage renal disease. Two case studies in this article describe the diagnosis and management of cystinuria, the most common rare kidney stone disorder.

Keywords

Genetic kidney disease; tiopronin; disorders of amino acids; kidney stones; nephrolithiasis; urolithiasis

Kidney stones, particularly those that present in childhood, may be due to rare inherited metabolic disorders (see accompanying article on rare kidney stone disorders in this issue [Goldstein & Goldfarb, 2017]). Patients with these rare disorders have recurrent and often obstructive stone formation that can lead to chronic kidney disease and even end stage renal disease. There is often significant delay in the diagnosis of these disorders, and patients may have to undergo multiple urologic procedures for stone removal, which can have a significant impact on their quality of life. Given the severity and chronicity of these conditions and the associated risk of progressive renal injury, the importance of early diagnosis and appropriate management cannot be overemphasized. Here, we describe two cases that illustrate the diagnostic workup and medical-surgical management of cystinuria, the most common of the rare kidney stone disorders.

Case Study 1

Patient J.O., currently 42 years of age, consulted our practice seeking additional information about and optimal care of her rare kidney stone disorder. At the time of presentation, she had a long and complicated medical and kidney stone history.

At the age of 13 years, she had sudden onset of sharp pain in her back and lower abdomen that worsened over a short period of time. She described an inability to find a comfortable position, nausea, vomiting, and intense sweating, and was brought to the emergency room with concern for ruptured appendicitis. In the emergency department, an abdominal X-ray revealed a right-sided ureteral stone 4 mm in diameter. She was told to take pain medication and was sent home for the stone to pass and be collected.

J.O.'s pain resolved, presumably representing passage of the stone. However, the stone was not recovered. She remained without incident until age 22, when she presented to the emergency department with the same symptoms as in the previous episode. The stone was collected and sent to the appropriate laboratory to determine its composition by X-ray crystallography. The stone composition was 100% cystine, and a diagnosis of cystinuria was made.

Clinical Interaction

J.O. was referred to a urologist and was told to increase her fluid intake. She was prescribed sodium bicarbonate and potassium citrate to be taken by mouth daily. Unfortunately, she was not counseled or did not understand she had a genetic stone disorder, which could lead to chronic and recurrent stone production. She continued to produce one to two stones per year, and at age 24, had multiple failed extracorporeal shock wave lithotripsies. Her surgeon proceeded with ureteroscopy, which was successful in making her stone-free.

Postoperatively, no changes were made to her medication regimen, and 24-hour urine testing was not considered. The pattern of passing one to two stones per year continued until age 30, when the patient began passing small fragments daily and experiencing chronic low-grade pain. She was found to have large bilateral stones requiring her first percutaneous nephrolithotomy (PCNL) procedure. Over the next four to five years, J.O. was in and out of the hospital with multiple pain episodes due to obstructing stones, some of which required urologic interventions.

In 2007, J.O. visited a new urologist, who performed her first 24-hour urine collection and noticed that the patient's cystine concentrations remained high despite attempts to increase fluid intake and alkalinize her urine. She was prescribed tiopronin (Thiola®) 200 mg twice daily, and was instructed to limit her sodium and protein intake. The urologist also provided J.O. with information regarding cystinuria as a genetic disorder.

Results of Clinical Interaction

J.O. described feeling optimistic about being offered a new drug for stone prevention. She also changed her diet and significantly increased her fluid intake. J.O. continued to follow up with the urologist for the next nine years. During that time, she had fewer stone episodes, but still continued to have at least one surgery per year and experienced chronic pain treated with opiates as needed. She was told that this type of lifestyle is expected, and it would be unlikely for her to become stone-free. She does not recall having more than one additional 24-hour urine collection during this time period. During her lifetime, J.O. underwent approximately 50 urologic procedures.

In mid-2015, J.O. interacted with the International Cystinuria Foundation, where she learned more about cystinuria and received a more detailed explanation regarding the use of tiopronin and the steps needed to become stone-free. Specifically, it was suggested that she see a local urologist who had more experience with cystinuria. She learned she may benefit by having her tiopronin dose adjusted so it would lower her cystine levels below the solubility limit (as per the prescribing information for tiopronin).

Two months later, the new urologist repeated J.O.'s 24-hour urine collection and detected persistently high concentrations of cystine. This finding justified an increase in her tiopronin dose to 600 mg three times daily. J.O. now reports little to no daily stone fragments in her urine, far less pain, and feeling better overall. Continued follow up on the patient's daily quality of life and results of imaging studies to assess her stone production are needed. More frequent 24-hour urine testing should be continued to assess her response to medication therapy and dietary management.

Clinical Implications

As described earlier, J.O. has had multiple surgeries. She describes developing chronic pain in her flank and back at the site of the surgeries. Fortunately despite all of these episodes of obstruction and procedures, she still has normal kidney function. J.O. takes medications daily for her disease and tolerates these drugs well (effects of cystinuria-specific medications vary from patient to patient).

J.O. has not always had the attentive care she desires and deserves. She has had many occasions where healthcare providers did not recognize the chronicity and recurrence of cystinuria. Further, her chronic pain was often downplayed and not always taken seriously if an obstructing stone was not seen on imaging studies. Understanding the chronic nature of cystinuria and recognizing that these patients have real pain may help improve the quality of care for patients with cystinuria (Modersitzki, Pizzi, Grasso, & Goldfarb, 2014).

J.O. struggles with chronic renal, back, and flank pain. She finds it difficult to plan for personal events and suffers from anxiety as a result. Her pain affects her ability to be a reliable parent and wife. Cystinuria has had a major impact on her quality of life.

Conclusion

This case describes an unfortunate but common situation for patients living with cystinuria, who are often under-informed about their disease and eagerly seek more information. In some cases, patients may be undergoing medical management but have not had adequate follow up with 24-hour urine collection to assess cystine levels and the effectiveness of their therapy. Patients are often not offered tiopronin when needed or are prescribed doses lower than the 800 mg/day as recommended in the prescribing information. J.O.'s experience and other similar patient histories lead to some critical conclusions about the management of cystinuria. To achieve success in the treatment of cystinuria, it is necessary to educate patients about their disease, review their stone history to determine appropriate medical management, and monitor patients adequately to assess the effectiveness of therapy, with the goal of rendering patients stone-free.

Case Study 2

Patient L.S. was healthy until age 13 years. Due to some mild abdominal discomfort, which in retrospect was not related to kidney stones, he visited an emergency department. During the initial emergency department visit, a plain film of the abdomen was performed, which demonstrated several large and asymptomatic radio-densities overlying both kidneys. Although the radiologist called the stones "calcifications," he had no way to confirm their

composition was actually calcium; in fact, it was not. L.S.'s urinalysis at that time showed a urine pH of 6.5, no protein, and no red or white blood cells. The urinalysis also revealed six-sided crystals, which are definitively diagnostic of cystinuria. L.S. was referred to his pediatrician, who ordered a 24-hour urine collection. The screening test for cystine was positive, and the patient was shown to have elevated levels of cystine and three dibasic amino acids: ornithine, arginine, and lysine. The mnemonic "COAL" or "COLA" is useful to recall the affected amino acids in cystinuria.

Later that year, L.S. experienced his first episode of renal colic. He returned to the emergency room, where a computed tomogram (CT) scan showed a 6 mm right distal ureteral obstructing stone.

Clinical Interaction

Ureteroscopy was performed and the stone removed. The right kidney contained several partial staghorn stones that extended into multiple renal calyces. The stones were removed by multiple PCNL procedures.

L.S. was told to increase his fluid intake to 4 L per day, restrict sodium intake to reduce cystine excretion, and limit protein intake to 100 g per day to reduce cystine and acid excretion. He was also prescribed potassium citrate 30 mEq by mouth after each meal and tiopronin 600 mg twice a day. On this regimen, his 24-hour urine collection showed 3.6 L of urine, pH 7.6, 120 mEq of sodium, and cystine excretion of 940 mg per day.

As a result of the stones, the local obstruction of multiple calyces, and multiple urologic procedures, kidney function on the right side was severely reduced. While L.S.'s serum creatinine was 1.1 mg/dL, a nuclear renal scan demonstrated that his left kidney was larger than the right and responsible for 91% of his total glomerular filtration rate (GFR) (see Figures 1 and 2). The relative lack of kidney function on the right side was evident on several occasions in L.S.'s early 20s. Over the course of two years, L.S. had four episodes of left renal colic, which were notable for creatinine increasing from normal values to 4.0 to 8.0 mg/dL. Each episode of acute kidney injury was caused by obstructive uropathy affecting the kidney that was responsible for most of his remaining total GFR. In each instance, a left ureteral stent was placed, relieving acute obstruction and returning serum creatinine to baseline values. On two occasions, L.S. was told that hemodialysis would be required, but rapid stent placement led to immediate recovery of kidney function.

Given the failure of medical therapy to prevent stone formation and the resulting kidney failure, the urologist constructed an ileal ureter. In this procedure, a loop of bowel was anastomosed from the renal pelvis to the bladder to serve as a wider ureter.

Results of Clinical Interaction

Ten years later, the patient has never been admitted to the hospital again. He occasionally notes small stones or gravel passed during urination. He remains on a sodium- and protein-restricted diet, potassium citrate for urine alkalinization, and tiopronin to minimize stone formation in the left kidney. His estimated GFR is excellent, with a serum creatinine concentration of 1.0 mg/dL.

Clinical Implications

This case illustrates several important issues in the care of patients with cystinuria. Most significant is that rare genetic causes of stones are often associated with reduced kidney function. In this case, the patient lost function in the right kidney and was at risk for losing function in the left kidney as well. In the modern era of advanced minimally invasive urology, chronic kidney disease is still common in cystinuria, and end stage kidney disease requiring dialysis or transplantation, although rare, still occurs. Early identification of cystinuria should lead to early medical therapy, which may help avoid more severe stone production and its sequelae. However, some patients first present with significant stone burden, and medical therapy may not be adequate. Innovative surgical approaches may help salvage kidney function and avoid the need for renal replacement therapy.

Conclusion

In the management of rare kidney stone disorders such as cystinuria, it is important not only to institute medical therapy promptly to reduce stone production, but also to assess the potential impact of these stones on renal function. Early recognition of kidney injury resulting from recurrent obstructive stone formation can help delay or prevent the development of end stage renal disease.

Acknowledgments

This work was supported in part by the Rare Kidney Stone Consortium (U54KD083908), which is a part of the NIH Rare Diseases Clinical Research Network, supported through collaboration between the NIH Office of Rare Diseases Research at the National Center for Advancing Translational Sciences and National Institute of Diabetes and Digestive and Kidney Disease. The authors also appreciate discussion with Dr. Ross Goldstein.

References

Goldstein R, Goldfarb DS. Early recognition and management of rare kidney stone disorders. Urologic Nursing. 2017; 37(2):81–89. 102. DOI: 10.7257/1053-816X.2017.37.2.81 [PubMed: 29240373]

Modersitzki F, Pizzi L, Grasso M, Goldfarb DS. Health-related quality of life (HRQoL) in cystine compared with non-cystine stone formers. Urolithiasis. 2014; 42(1):53–60. [PubMed: 24253538]

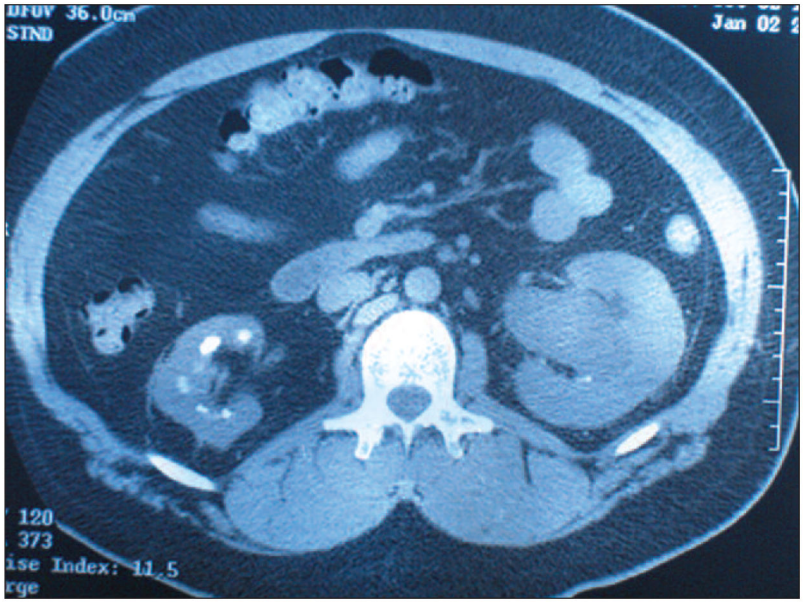

Figure 1.
The right kidney is small with several stones and very little renal parenchyma. The left kidney has significant hydronephrosis.

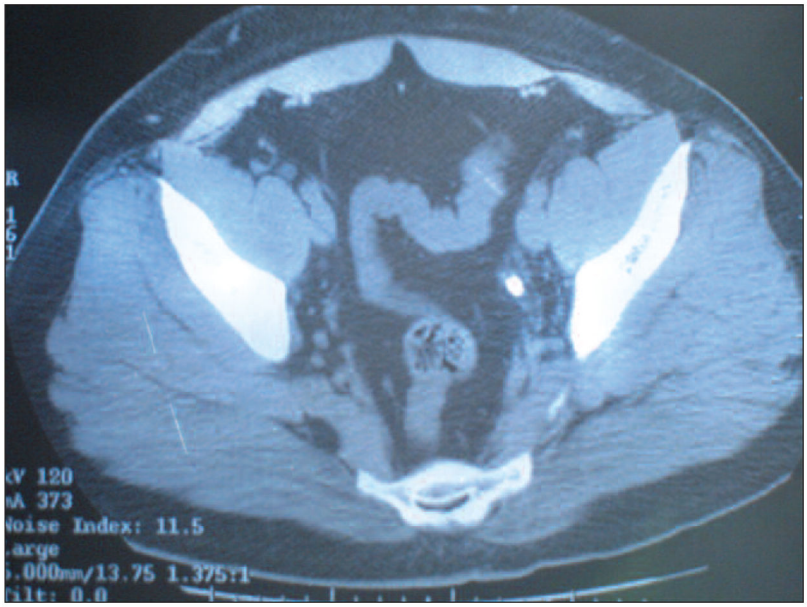

Figure 2.

An image from the same CT scan as seen in Figure 1. This pelvic view demonstrates a left, distal ureteral stone, which is responsible for the hydronephrosis seen in Figure 1.