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CLINICAL VIGNETTE

A Case of Acute Kidney Injury due to Oxalate Nephropathy

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Case Summary

A 61-year-old man with history of colon cancer s/p right hemicolectomy with recurrence found in the root of the mesentery 3 years later s/p small bowel resection with 2-3 feet of small intestine remaining complicated by short bowel syndrome, iron deficiency, and CKD stage 3 was referred for nephrology evaluation 5 years after his initial diagnosis of colon cancer for progressively worsening renal function. His serum creatinine was 3.15 mg/dL compared with a baseline of 2.2-2.5 mg/dL throughout the year prior. He had a good appetite, but complained of excessive thirst and was drinking 2-2.5 liters of fluid per day. He urinated 3 to 5 times per night without weak urinary stream, dysuria, or feeling of incomplete void. The patient denied any recent nausea, vomiting, or diarrhea. He did not use NSAID chronically and had no history of kidney stones. He did not have family history of kidney disease. Medications included ergocalciferol 50,000 IU weekly and a multivitamin.

Vitals signs showed a temperature 97.7°F, blood pressure 90/57, heart rate 64 beats/min, respiratory rate 16 breaths/min, oxygen saturation 97% on room air, and a body mass index 20.15 kg/m^2. Physical examination revealed a pleasant man in no distress. Lungs were clear to auscultation bilaterally. His abdomen had normal bowel sounds without tenderness, rebound, guarding, or masses. He had no lower extremity edema bilaterally. He had moist oral mucosa, no elevation in the jugular venous pulse, and normal skin turgor.

Laboratory studies included a basic metabolic panel remarkable for total CO2 16 mmol/L with an anion gap of 15, BUN 48 mg/dL, and creatinine 3.15 mg/dL. CBC showed a mild normocytic anemia. Liver tests showed an albumin 3.8 g/dL, AST 55 U/L, and ALT 112 U/L with normal alkaline phosphatase and bilirubin. Urinalysis was significant for 2+ leukocyte esterase and WBC 11-30/hpf. Urine total protein/creatinine ratio was 0.1. Serum and urine protein electrophoresis, anti-streptolysin O antibody, ANCA, ANA, double stranded DNA antibody, C3, C4, quantiferon gold, rheumatoid factor, and anti-glomerular basement membrane antibody were negative. Serologic testing was negative for HIV, hepatitis B, hepatitis C, and syphilis.

Sodium bicarbonate 650 mg PO BID was initiated for the non-gap metabolic acidosis. Weekly serum creatinine levels were checked with initial improvement (2.97, 2.92, and 2.84 mg/dL) until it began to rise again (3.5 and 3.86 mg/dL).

Due to worsening renal function, a kidney biopsy was obtained and showed:

1. Acute tubular injury with intraluminal calcium oxalate deposition.
2. Focal interstitial inflammation with scattered interstitial eosinophils.
3. Arterial and arteriolar nephrosclerosis with features of glomerular ischemia.
4. Approximately 35% global glomerulosclerosis with mild overall parenchymal scarring.

Discussion

Our patient was diagnosed with acute kidney injury due to oxalate nephropathy in the setting of enteric hyperoxaluria (EH) from short bowel syndrome. Fat malabsorption leads to increased fatty acid delivery to the colon. The free fatty acids bind to dietary calcium with less dietary calcium available to precipitate dietary oxalate. In addition, the fatty acids and unabsorbed bile acids increase colonic permeability to small molecules including oxalate. The result is an increase in oxalate absorption. Patients with short bowel syndrome frequently have diarrheal fluid losses leading to decreased urine volume, metabolic acidosis, a low urine pH, reduced urine citrate excretion, and urinary supersaturation of calcium oxalate. One study showed patients with ileal resection and hyperoxaluria absorb five times as much 14C oxalate as control subjects.[1] Other than intestinal resection for bowel disease, causes of EH in adults include bariatric surgery, celiac disease, pancreatic insufficiency, and orlistat therapy.

Several strategies are used in the management of EH, none of which have been tested in randomized control trials. The most important is high fluid intake to increase daily urine output >2 to 3 liters, which lowers the supersaturation of calcium oxalate.[2]

Other dietary modifications used to treat EH include limiting dietary oxalate and fat intake. One study of four patients showed that a low oxalate diet (<4 mg of oxalate per 24 hours) promptly abolished hyperoxaluria.[1] High oxalate-containing foods include spinach, rhubarb, nuts, chocolate, cornmeal, okra, potato chips, avocados, and beets. High dietary intake of vitamin C has also been associated with hyperoxaluria. Ascorbic acid is oxidized to dehydroascorbic acid, then to diketogulonic

acid, and catabolized to oxalate, which is excreted in urine in amounts proportional to intake of ascorbic acid.[3]

The addition of calcium supplements has been effective in the treatment of EH. Calcium supplements increase free intestinal calcium that binds to dietary oxalate in the intestinal lumen to prevent its absorption. One study of 8 patients with EH and fixed standardized diets of calcium, oxalate, and fat were given an additional 1 gram of calcium supplementation.[4] Renal oxalate excretion decreased from 119 mg/24 h to 60 mg/24 h with decreased colonic oxalate absorption from 28% to 9% with no increase in urinary calcium.

Hypocitraturia is also common in patients with EH. It is caused by bicarbonate losses from chronic diarrhea and results in metabolic acidosis. While potassium citrate and potassium bicarbonate are frequently used, sodium citrate and sodium bicarbonate can be used with caution since their use leads to an increase in sodium excretion and an associated increase in calcium excretion.

Bile acid sequestrants can also be used since they bind and prevent the absorption of oxalate and bile acids. They should also be used with caution as they may worsen steatorrhea, resulting in malabsorption of folic acid and fat-soluble vitamins.[5]

Our Patient

Our patient initiated a low fat, low oxalate diet on his own before a 24-hour urine collection could be performed. Of note, he stopped eating corn meal, peanut butter, and spinach. Fluid intake was increased to 120 fluid ounces per day. His creatinine peaked at 3.92 mg/dL and improved to 3.38 mg/dL within one week and his pyuria resolved. 24-hour urine collections found persistent hypocitraturia without hyperoxaluria. Treatment with calcium citrate 1000mg TID with meals in addition to sodium bicarbonate 650mg BID was initiated. It has now been 2 years since his kidney biopsy and his creatinine has slowly improved back to his previous baseline (2.40 mg/dL).

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