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Case study

Acute oxalate nephropathy due to pancreatic atrophy in newly diagnosed pancreatic carcinoma☆,☆☆,★

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Summary Acute oxalate nephropathy can occur due to primary hyperoxaluria and secondary hyperoxaluria. The primary hyperoxalurias are a group of autosomal recessive disorders of endogenous oxalate overproduction. Secondary hyperoxaluria may occur as a result of excess dietary intake, poisoning with oxalate precursors (ethylene glycol), or enteric hyperoxaluria. The differential diagnosis of enteric hyperoxaluria includes inflammatory bowel disease, short bowel syndrome, bariatric surgery (with jejunoileal bypass or Roux-en-Y gastric bypass), celiac disease, partial colectomy, and chronic pancreatitis. The common etiology in all these processes is fat malabsorption, steatorrhea, saponification of calcium, and absorption of free oxalate. Hyperoxaluria causes increased urinary oxalate excretion, urolithiasis (promoted by hypovolemia, decreased urinary pH caused by metabolic acidosis, and decreased citrate and magnesium concentrations in urine), tubulointerstitial oxalate deposits, and tubulointerstitial nephritis. We report a rare case of acute oxalate nephropathy due to pancreatic atrophy and exocrine insufficiency caused by newly diagnosed pancreatic cancer.

1. Introduction

Secondary hyperoxaluria is usually the result of conditions that are characterized by increased intestinal oxalate absorption, including a high-oxalate diet, fat malabsorption (enteric hyperoxaluria), alterations of the intestinal oxalate-degrading microorganisms, and genetic variations of the intestinal oxalate transporter. Hyperoxaluria caused by malabsorption occurs due to increased intestinal oxalate absorption because excess free fatty acids in the intestinal lumen bind to calcium allowing free oxalate to be absorbed in the large bowel. In addition, bile salts and free fatty acid in the colon may increase permeability of the bowel wall and

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allow increased absorption of oxalate. Exocrine pancreatic insufficiency is a well-known cause of fat malabsorption and is increasingly being recognized as a cause of acute oxalate nephropathy [1,2].

Exocrine insufficiency frequently develops in patients with pancreatic cancer. In one study, almost half of all patients who were diagnosed as having pancreatic cancer had evidence of pancreatic exocrine insufficiency (by measuring fecal elastase) at the time of diagnosis; this exocrine insufficiency was attributed to tumor ingrowth and fibrosis/atrophy due to obstruction of the pancreatic duct [3]. Up to 30% of autopsies on patients with pancreatic cancer show evidence of pancreatic atrophy. Acinar tissue may be destroyed in 2 to 3 weeks after obstruction of ducts and undergoes atrophy and fibrosis without evidence of regeneration [4,5]. However, intestinal lipase can replace pancreatic lipase, and fat is split even in the absence of pancreatic lipase. Steatorrhea is thought to be caused by impaired absorption of cholesteryl esters due to lack of pancreatic cholesterase. Reduced protein breakdown prevents the absorption of fats because the intestine cannot make phospholipids [6].

Dietary oxalate is the precursor of urinary oxalate [7]. The degree of steatorrhea is directly correlated with the degree of hyperoxaluria and inversely correlated with dietary calcium [8]. The colon is the site of enhanced oxalate absorption [9]. Dehydration or renin-angiotensin-aldosterone system inhibitors exacerbate or increase oxalate absorption by increasing intratubular concentration of oxalate via reabsorption of sodium and water in the proximal tubule [10].

Although it has been established that pancreatic insufficiency causes steatorrhea, which results in saponification of calcium, hyperoxaluria, and increased urinary oxalate excretion, there is only one report of chronic kidney disease attributed to exocrine insufficiency in a patient with pancreatic cancer [11]. We report a rare case of acute oxalate nephropathy in a patient with newly diagnosed pancreatic cancer with computed tomographic (CT) evidence of pancreatic atrophy and exocrine insufficiency.

2. Materials and methods

The patient is a 66-year-old paraplegic woman with medical history of ovarian cancer, uterine cancer status post-hysterectomy with salpingo-oophorectomy, and colon cancer status post sigmoidectomy 2 years prior who was admitted for evaluation of nausea, vomiting, and diarrhea. Patient denied travel, exposure to pets, consumption of unpasteurized dairy or raw fish, recent antibiotic intake, joint pain, mouth ulcers, or eye redness. She complained that her stools were greasy and malodorous and would float on water. Initially, her emesis resembled oral intake but later was nonbloody, bilious in nature. Her oral intake was low because of the vomiting. Oral ondansetron did not alleviate the vomiting because oral ondansetron was poorly absorbed. Vomiting improved with intravenous ondansetron. She also had persistent diarrhea, which did not respond to antidiarrheal medications like loperamide. She was later started on pancreatic enzyme supplementation with improvement in diarrhea. Diarrhea also responded to cholestyramine. She denied nonsteroidal anti-inflammatory agents and recent iodinated contrast exposure. Patient denied urinary frequency, dysuria, or urgency. Patient denied symptoms of obstructive uropathy such as weak urinary stream, dribbling, or incomplete bladder evacuation.

CT of the abdomen revealed a mass in the pancreatic head with local invasion 1 month ago; pancreatic adenocarcinoma was confirmed with endoscopic ultrasound, fine-needle aspiration, and needle core biopsy of the pancreatic mass. Repeat CT of the abdomen without contrast showed pancreatic atrophy.

Her creatinine (Cr) 1 month prior to admission was 0.8 mg/dL. Her admission Cr was 10.4 mg/dL. Lipase was elevated at 248 U/L (8-78 U/L), but liver function test results were normal and international normalized ratio was 1.2. Renal ultrasound showed increased cortical echogenicity and accentuated cortical medullary differentiation.

Urine sodium was 97 mmol/L, urine Cr was 125.6 mg/dL and the fractional excretion of sodium was 5.6%. Urine eosinophils were 5% (normal < 1%), which is nonspecific but can be consistent with tubulointerstitial nephritis. Urinalysis showed protein of 300 mg/dL, red blood cells of 43/high-power field, white blood cells greater than 150/high-power field, and no bacteria. Urine protein-to-Cr ratio was 1.8 g/g. Microalbumin-to-Cr ratio was 410 mg/g. The urinary albumin-to-protein ratio was 0.22, consistent with tubular proteinuria. Ionized calcium was low at 0.97 mmol/L (1.13-1.3 mmol/L), calcitonin was suppressed at less than 2 pg/mL (0.0-5.1 pg/mL), and vitamin D was only modestly insufficient at 27 ng/mL (optimal concentrations 30-80 ng/mL). Antinuclear antibodies, antineutrophil cytoplasmic antibodies, hepatitis panel, anti–glomerular basement membrane antibodies, and complement serologies were all normal. Fecal pancreatic elastase was less than 50 μg/g.

The patient was volume resuscitated adequately for 3 days with no significant improvement in renal function. A renal biopsy was performed demonstrating acute on chronic tubulointerstitial nephritis with calcium oxalate crystals in the tubules consistent with oxalosis (Figs. 1 and 2). Examination of the biopsy specimen revealed one core of renal corticomedullary tissue with approximately 7 to 11 glomeruli per level section, of which 2 to 3 per level section were globally sclerosed. The viable glomeruli had normal mesangial areas and thin and delicate capillary loops, and showed no inflammation, endocapillary proliferation, segmental sclerosis, or other specific abnormalities. Tubules showed patchy flattening of epithelium with loss of brush borders, enlarged nuclei, and prominent nucleoli. Some tubules contained prominent fan-shaped, clear-to-yellow birefringent crystals (Fig. 2). The intratubular calcifications