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Acute Renal Failure Due to Vitamin C: Case Report and Review of the Literature

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Case Report

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Abstract

Background: Vitamin C is an essential dietary nutrient that is necessary for normal growth and development. The endpoint product of vitamin C metabolism, oxalate, is excreted by the kidney and is nephrotoxic. Deposition of oxalate crystals in renal tubules can cause tubular necrosis and result in acute renal injury.

Case Presentation: This article presents an 80-year-old patient with acute renal failure due to oxalate nephropathy associated with oral vitamin C intake and reviews oxalate nephropathy. Our case emphasizes renal function monitoring in patients receiving long-term vitamin C especially with a history of renal disease. Over consumption of vitamin C can lead to acute kidney injury. Patients under nephrotoxic treatments are at risk for acute kidney injury from a high vitamin C diet and should be suspected in unexplained renal insufficiency.

Conclusion: Careful review of diets and all medications is necessary when confronted with unexplained renal insufficiency. Closely monitoring renal function is recommended in patients on high vitamin C.

Keywords: Vitamin C; Acute Renal Failure; Oxalate Nephropathy

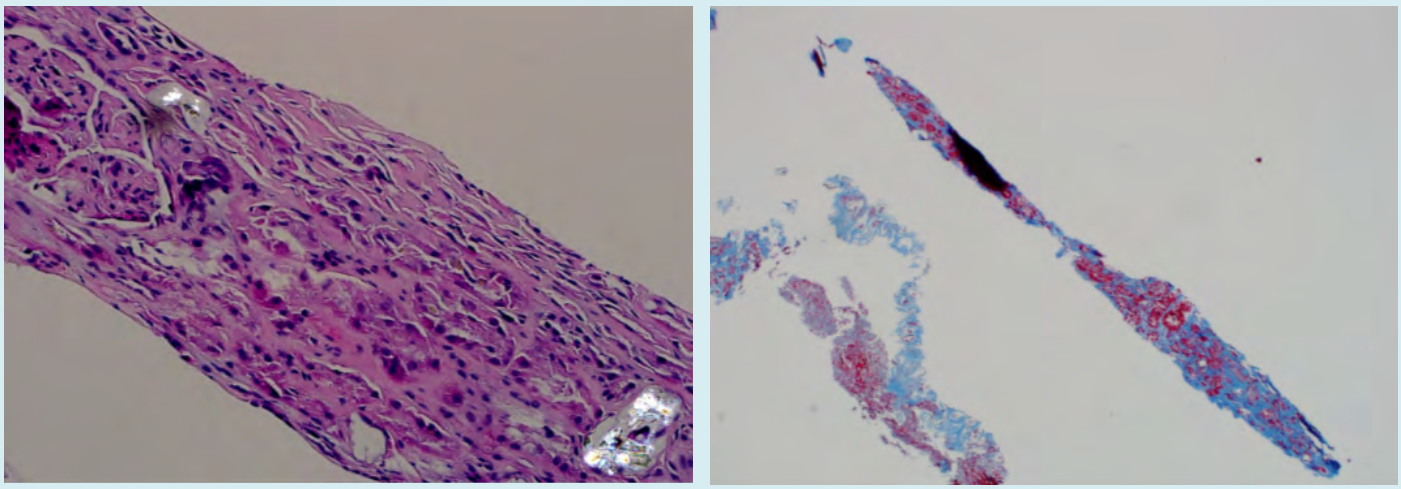
Introduction

Vitamin C (ascorbic acid) is a water-soluble essential nutrient identified in the 1930s as a consequence of the search for a substance, the deficiency of which causes scurvy. It has been hypothesized that Vitamin C may reduce the incidence of most malignancies in humans [1] probably through its antioxidant properties including the neutralization of free radicals [2,3]. First studies showed that high-dose intravenous vitamin C increased the average survival of advanced cancer patients [4-6]. However, subsequent studies didn't reproduce that benefit [7,8]. Oxalate is a major end product of ascorbic acid metabolism, which is excreted in urine [9-11]. Previous reports have described the acute oxalate nephropathy in association with excessive vitamin C intake of greater than 2 grams/day. Here we present a cancer patient with oxalate-induced acute renal failure that was attributable to consumption of vitamin C supplement. We discuss the cause of calcium oxalate nephropathy following a review of the literature.

Case Report

An 80-year-old Caucasian man with past medical history of metastatic cholangiocarcinoma presented to our emergency department with complaints of nausea, vomiting, and inability to orally intake over the past several days. His disease was stable with no active treatment for his cancer for the last year. He had elevated bilirubin which was related to a biliary stent malfunction. He underwent stent exchange with improvement. On physical examination, he appeared volume depleted. Body temperature, blood pressure, pulse rate, respiratory rate, and SpO2 on room air were 36.5 °C, 163/69 mmHg, 50 beats/min, 18 breaths/min, and 99%, respectively. His buccal mucosa was dry. There was a mild tenderness with deep palpation of the epigastric region. The physical examination was otherwise unremarkable. His family history was unremarkable. The rest of his medical history included coronary artery disease with the history of CABG, previous upper respiratory infection, and right rotator cuff injury. The patient never had any prior kidney disease. His medication included thyroid supplementation, multivitamin, vitamin B and vitamin C two grams daily.

On admission, his laboratory tests showed WBC count 6.0 k/ul, hemoglobin 10.3g/dl, platelet count 250K/ul, BUN 88mg/dl, and creatinine 7.03mg/dl (baseline creatinine 0.65mg/dl), Sodium 122meq/L, potassium 6meq/L, chloride 91meq/L, carbon dioxide 20meq/L, magnesium 2.6meq/L, total bilirubin 2.5mg/dl, indirect bilirubin 1.5mg/dl, direct bilirubin 1mg/dl, alkaline phosphatase 575 IU/L, LDH 615IU/L, and ALT 54IU/L, AST 44IU/L, total protein 6.7, albumin 3.4g/dL, calcium 8.4meq/L, phosphorus 8meq/L, and glucose 66mg/dl. His urinalysis revealed trace protein and leukocyte esterase, 2-5 RBCs per high power field, and 2-5 WBCs per high power field. Ultrasonography of kidneys showed normal sized kidneys with no hydronephrosis. There was an abnormal appearance with prominent pyramids and increased echogenicity in the renal parenchyma. Upon admission, he was initiated intravenous hydration 150 mL of normal saline per hour, kayexalate 30 grams for two doses, and Zosyn 2.25grams intravenous every 8 hours. Despite aggressive intravenous hydration, the level of serum creatinine did not improve and increased to 8.7 mg/dL, therefore he underwent hemodialysis and continued to require it for three months at which point had renal recovery. A renal biopsy was performed and revealed mild to moderate tubulointerstitial fibrosis with numerous calcium oxalate crystals with an average of approximately 6 crystal deposits present per glomerulus (Figures 1A & 1B).



A **B**

Figure 1A: H&E-cross polarized light: focal birefringent crystals consistent with calcium oxalate.
Figure 1B: Trichrome: mild to moderate interstitial fibrosis.

Discussion

Oxalate arises in the body from a combination of dietary sources and endogenous production from precursors. Hyperoxaluria considered being a primary risk factor for calcium oxalate stones, which are present in up to 75% of patients diagnosed with renal lithiasis [12,13]. Additionally it may cause deposition of calcium oxalate crystals in the kidney and result in the variable degrees of atrophy and inflammatory reaction. In setting of decreased tubular flow calcium oxalate crystals causes luminal obstruction with an increase in cytokine release leading to cell death, tubular atrophy and eventual fibrosis. With decreased calcium oxalate clearance perpetuates for further precipitation

in the tubules and continued irreversible damage [14]. Oxalate crystals are injurious to renal epithelial cells via the generation of free radicals [15-17] and inducing apoptosis [18,19]. Therefore based on the etiology and hyperoxaluria severity, the presentation is different, from kidney stones to renal failure and other tissue depositions (oxalosis).

Hyperoxaluria is classified as either primary or secondary. Primary hyperoxaluria (PH) is a rare autosomal recessive inherited disorder of the glyoxylate metabolism in the liver and is classified to PH I-III based on the enzyme defect. It is characterized by renal failure, progressive deposition of diffuse calcium oxalate crystals, and severe recurrent kidney stones. Secondary hyperoxaluria may occur as a result of excess dietary intake, increased endogenous production, or decreased excretion (Figure 2). Secondary hyperoxaluria can occur by one or more of these mechanisms:

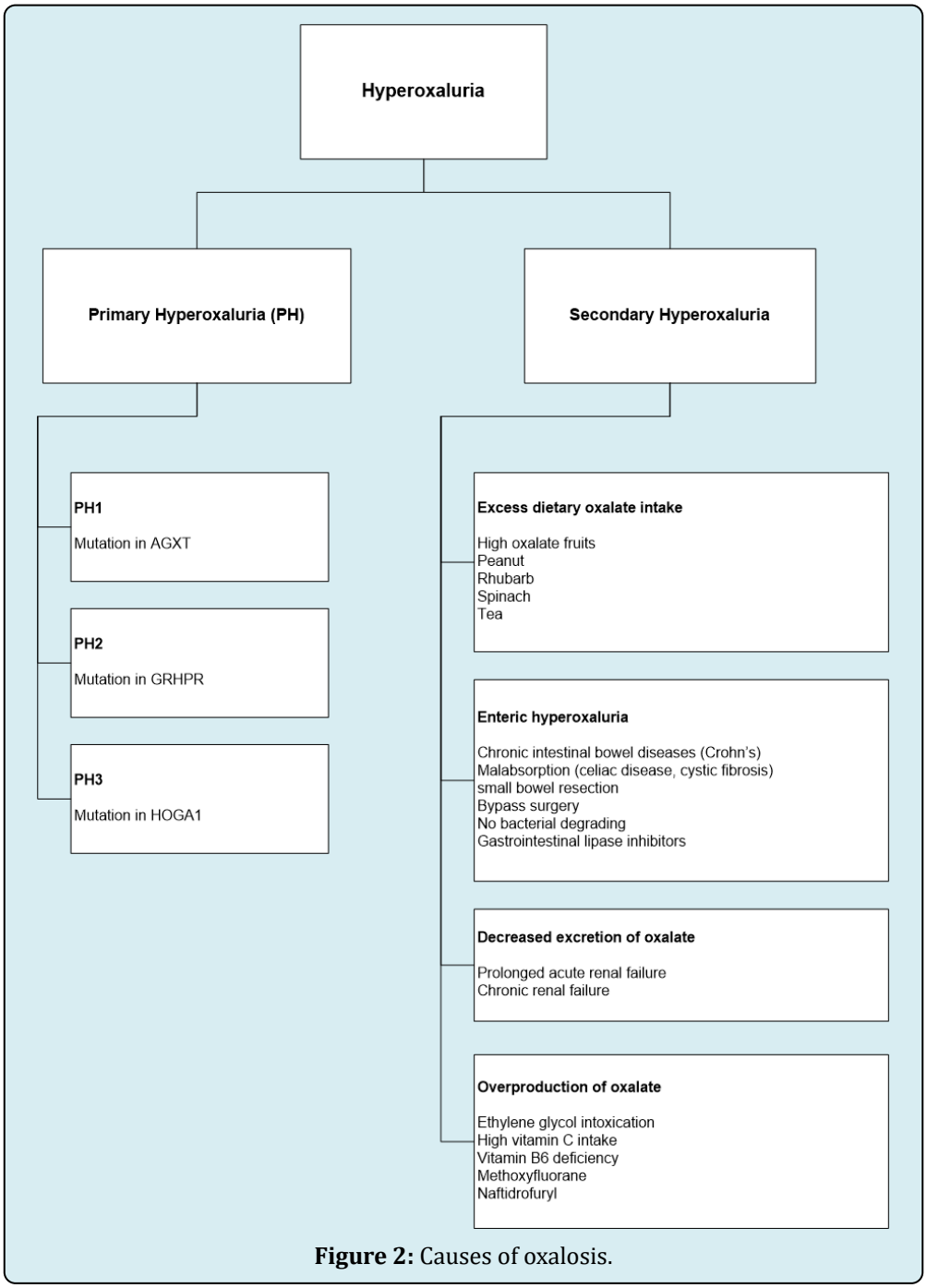


Figure 2: Causes of oxalosis.

Excess Dietary Oxalate Intake

Oxalate is a natural component of fruits and vegetables. Increase in oxalate serum levels and hyperoxaluria can occur upon increased dietary ingestion of foods with high oxalate content [20-24]. Several reports describe excessive fruit juice ingestion leading to hyperoxaluria and subsequent acute oxalate nephropathy [25-28]. Also, there are some reports on oxalate nephropathy due to excessive peanut [29] or rhubarb [30,31] intake.

Enteric Hyperoxaluria

Enteric hyperoxaluria was first described in patients with small bowel resection who subsequently began to develop recurrent calcium oxalate stones in their urinary tract [32]. It has been reported in certain intestinal diseases like chronic inflammatory bowel disease [33-36], celiac disease [37,38], Roux-en-Y gastric bypass surgery [39-42] and orlistat therapy [43-46] and showed that can lead to end-stage renal disease requiring kidney transplantation [47,48].

Calcium normally binds to oxalate in the intestinal lumen leading to fecal elimination of calcium oxalate. In malabsorption, excessive intraluminal free fatty acids competitively bind to the intraluminal calcium ions and thereby allow unbound oxalate to be absorbed in colon [49,50]. In addition, bile salts and free fatty acids are toxic to colonic mucosa and may increase oxalate absorption by increase the permeability of colonic wall [51].

In addition, oxalate is metabolized by Oxalobacter formigenes, gram-negative anaerobic bacteria that colonizes the gastrointestinal tract [52,53]. O. formigenes is sensitive to a variety of antibiotics [54] and its low count after antibiotic therapy may cause hyperoxaluria by increasing oxalate absorption.

Decreased Excretion of Oxalate

The kidney is the primary organ for oxalate excretion via glomerular filtration and tubular secretion (mediated via SLC26 anion exchangers) [55-57]. It has been shown that serum oxalate level is elevated about 10 fold in patients with chronic renal failure (uremic oxalosis) due to decrease oxalate clearance [58-60]. In addition, dialysis patients tend to lose ascorbic acid during dialysis and as a result, should receive vitamin C supplementation [61]. Subsequently, there have been reports of cases of patients on dialysis who developed oxalate crystal deposition in various organs secondary to vitamin C supplementation [62]

Overproduction of Oxalate

Endogenous production of oxalate precursor, glyoxylate, occurs in liver by oxidation of glycolate or by catabolism of hydroxyproline, a component of collagen. This mechanism is associated with hyperoxaluria in ethylene glycol intoxication [63,64]. Overproduction of oxalate may occur due to high doses of vitamin C, which is a precursor of oxalate, or vitamin B6 (cofactor of AGT enzyme) deficiency [65]. Vitamin C has been shown to have antioxidant effects as a free radical scavenger. Vitamin C has a protective effect against drug-induced nephrotoxicity [66,67]. However, excessive use and in setting of renal injury, there are several reports on hyperoxaluria and nephropathy due to intravenous high dose of vitamin C [68-70]. Further reports showed that hyperoxaluria and nephropathy can be associated with high dose oral vitamin C [71-73], but may even occur in regular doses [74]. In the setting or regular doses of Vitamin C the toxicity of vitamin C can be further compounded with renal insufficiency [14,75].

Vitamin C is one of the most popular over-the-counter supplements (http://newhope360.com/2012-supplement-business-report). Vitamin C is widely used in various diseases from the common cold to cancers. It is also widely used by alternative medicine practitioners as a treatment for various diseases and conditions [76,77]. After the first studies showing benefits of vitamin C in cancer patients [4,5] it is frequently used as a treatment in alternative medicine.

Volume depletion, hypomagnesemia, metabolic acidosis, and reduced urinary citrate excretion are causes of oxalate precipitation. Our patient volume depletion at the time of presentation that together with long-term vitamin C intake cause oxalate nephropathy.

Conclusions

Our case emphasizes the importance of close monitoring of renal function in chronic vitamin C users. Additionally physicians should be aware of vitamin C effects on the kidney and use it with caution in patients with pre-existing renal disease, those who receive nephrotoxic medications, and patients with a history of oxalate nephrolithiasis.

Acknowledgment: None

Consent

The patient reported here is deceased and we have unsuccessfully attempted to contact the next of kin. In order to preserve confidentiality, the report is de-identified and no identifiable information or pictures are being submitted.

Competing Interests

The authors report no competing interests. All authors consents to publication and give permission to publish.

Authors Contributions

MG contributed to care of the patient. AA and WG were specialty consultants. AH and AA did the literature review. All authors participated in drafting, revision and editing of the manuscript.

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