

## Case Report

# Vitamin C-Induced Oxalate Nephropathy

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Although a multitude of syndromes have been thoroughly described as a result of vitamin deficiencies, over consumption of such substances may also be quite dangerous. Intratubular crystallization of calcium oxalate as a result of hyperoxaluria can cause acute renal failure. This type of renal failure is known as oxalate nephropathy. Hyperoxaluria occurs as a result of inherited enzymatic deficiencies known as primary hyperoxaluria or from exogenous sources known as secondary hyperoxaluria. Extensive literature has reported and explained the mechanism of increased absorption of oxalate in malabsorptive syndromes leading to renal injury. However, other causes of secondary hyperoxaluria may also take place either via direct dietary consumption of oxalate rich products or via other substances which may metabolize into oxalate within the body. Vitamin C is metabolized to oxalate. Oral or parenteral administration of this vitamin has been used in multiple settings such as an alternative treatment of malignancy or as an immune booster. This article presents a clinical case in which ingestion of high amounts of vitamin C lead to oxalate nephropathy. This article further reviews other previously published cases in order to illustrate and highlight the potential renal harm this vitamin poses if consumed in excessive amounts.

## 1. Introduction

Acute renal failure can occur as a result of acute tubular necrosis secondary to acute oxalate nephropathy due to the deposition of calcium oxalate crystallization within the renal tubules [1]. Oxalate nephropathy can occur in both primary and secondary hyperoxaluria. Primary hyperoxaluria is a group of autosomal recessively inherited enzymatic deficiencies that lead to the increased urinary excretion of oxalate. In Type 1 primary hyperoxaluria, there is a reduction of alanine:glyoxylate aminotransferase (AGT) activity in the liver, leading to an accumulation of oxalate [2]. Type 2 primary hyperoxaluria involves a mutation of glyoxylate reductase/D-glycerate dehydrogenase, leading to the excretion of increased amounts of L-glyceric acid as well as oxalate [3].

Secondary hyperoxaluria can occur due to increased dietary oxalate intake, increased absorption of oxalate from the bowel (also known as enteric hyperoxaluria), and increased production of oxalate.

Increased dietary intake of oxalate is fairly uncommon; however, there have been case reports in the literature

describing excessive star fruit juice ingestion [4, 5] and peanut intake [6] leading to oxalate nephropathy. Enteric hyperoxaluria results mainly from fat malabsorption, which leads to increased absorption of soluble oxalate from the colon. Calcium binds to the free fatty acids that cannot be absorbed. This reduces the normal calcium oxalate precipitation in the feces thereby allowing the absorption of soluble oxalate. This mechanism of enteric hyperoxaluria is manifested in several ways, including with orlistat therapy [7, 8], Roux-en-Y gastric bypass surgery [9], celiac disease, and Crohn's disease. Increased production of oxalate is mainly due to increased levels of oxalate precursors, more commonly glyoxylate, which is associated with ethylene glycol ingestion, and less commonly ascorbic acid [10]. We report, in detail, a case of a patient who presented with this rare occurrence of excessive vitamin C-induced oxalate nephropathy.

## 2. Case Presentation

Our patient is a 72-year-old white male who was brought to the emergency department after being found down at home and confused. On presentation, he was found to have

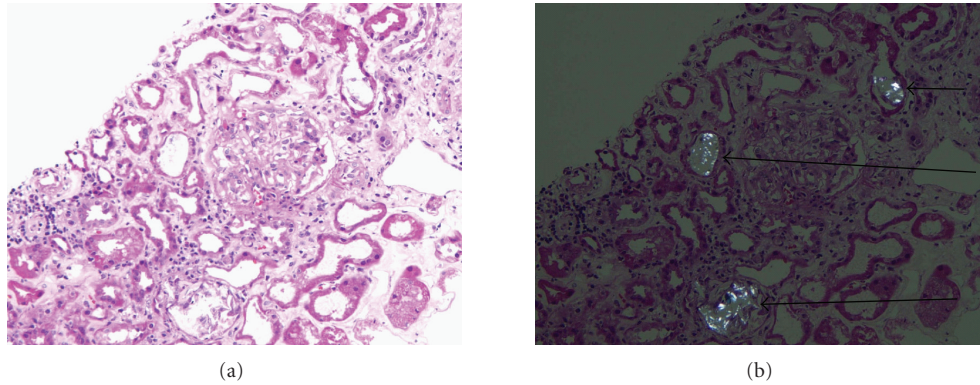


FIGURE 1: (a) shows renal cortex with acute tubular injury. (b) depicts the same area under polarized light. The arrows indicate the deposition of calcium oxalate crystals. H&E,  $\times 200$ .

TABLE 1: Summary of biopsy proven cases of oxalate nephropathy secondary to ascorbic acid reported in the literature.

Patient (Ref. Num.)*	Age	Gender	Baseline Serum creatinine (mg/dl)	Renal presentation and serum creatinine (Cr) in mg/dl	Dose of ascorbic acid per day	Duration of administration	Treatment	Outcome
20	71	Female	1.4	Anuria (Cr = 12.1)	500 mg (oral)	6 months	HD	ESRD
15**	58	Female	1.0	Oliguria (Cr = 3.5)	45 g (IV)	1 day	HD	Death
21***	72	Male	Unknown	Anuria (Cr = 15.3)	Grams (oral)	Months	Medical	Death
22	73	Male	1.2	Poor renal clearance (Cr = 8.4)	680 mg (oral)	4 months	HD	Recovery Cr = 1.8 mg/dl
23	31	Male	Unknown	Poor renal clearance (Cr = 10.1)	2.5–5.0g (oral)	Undisclosed (week to months?)	HD	Recovery Cr = 2.2 mg/dl
24	49	Female	0.7	Oliguria (Cr = 4.5)	4.0 g (oral)	Several months	HD	Recovery Cr = 1.1 gm/dl
10	58	Male	1.4	Anuria (undisclosed)	1 g (IV)	2 months	HD	Recovery Cr = 1.4 mg/dl
14	61	Male	1.3	Anuria (Cr = 13.3)	60 g (IV)	1 day	Medical	Recovery Cr = 2.9 mg/dl

\*The ref. num. identifies the individual case report. Please refer to the listed references at the end of the article to locate any particular case report by its reference number.

\*\*The patient died from multiple organ failure. Her systemic illness was amyloidosis.

\*\*\*The patient died from renal failure and associated multiple organ failure as he did not want to undergo dialysis.

a BUN level of 102 mg/dL, a creatinine level of 10.6 mg/dL (baseline BUN 3.6 mg/dL and creatinine 1.3 mg/dL), and was also found to be oliguric. An ABG in the emergency department showed a pH of 7.19, PCO<sub>2</sub> of 53, HCO<sub>3</sub> of 21.4, and a PO<sub>2</sub> of 77 mmHg on 2 liters of O<sub>2</sub> via nasal cannula. His acidosis was attributed to the patient's history of COPD and chronic CO<sub>2</sub> retention. Urinalysis in the emergency department showed 1 RBC/hpf, 1+ protein, and no WBC or microorganisms present. Urine toxicology was positive for prescribed opiates and negative for recreational substances, including cocaine, ethanol, and amphetamines. The patient's ethyl alcohol and salicylate levels were undetectable. His FeNa was calculated to be 1.7%. His measured serum osmolality was 321 mOsm/kg whereas his calculated osmolality was 3 mOsm/kg. Lab analysis also showed an elevated anion gap of 19.

Further history was difficult to attain given the fact that the patient was only alert to person but not to place or time. The patient was admitted to the medical ICU and the nephrology service was consulted for further evaluation. Due to his poor renal clearance, he was initiated on hemodialysis (HD).

The patient's mental status improved after about a week, and his kidney function continued to slowly improve. During his hospital stay, the patient was found to have negative p-ANCA, c-ANCA, and qualitative ANA values. The patient's C3 and C4 levels were within normal limits.

However, despite continued supportive therapy, the patient's kidney function had not significantly recovered as expected. A renal biopsy was performed to shed further light on his disease process. The pathology report of the renal biopsy was consistent with findings of oxalate nephropathy

as numerous tubules showed birefringent crystals shaped as plates or fine spicules under polarized light (Figure 1). There were also findings of moderate interstitial fibrosis, mild-to-moderate acute tubulointerstitial nephritis and mild hyaline and hyperplastic arteriolosclerosis with moderate-to-severe arteriosclerosis.

Upon further questioning, the patient denied ingestion of any products containing ethylene glycol or any medications other than what was prescribed to him. He also denied any prior gastric surgeries. However, the patient did mention that he had changed his eating habits within the past year as he wanted to include more leafy vegetables that incidentally were rich in oxalate. He also admitted to ingesting between 1.9 L and 3.8 L per day of his favorite beverage for about 3-4 months prior to presentation. This beverage was an orange flavored powder drink, which had about 60 mg of vitamin C per 236.6 mL serving. Therefore, the patient was ingesting approximately 480 mg to 960 mg of vitamin C daily. The patient's oxalate nephropathy was attributed to excessive vitamin C intake, which anecdotally has a poor prognosis. As the biopsy demonstrated significant interstitial inflammation, prednisone was started at 60 mg and tapered down for a period of six weeks. The patient was discharged from the hospital on HD. Five weeks after discharge, he was able to be dialysis independent. His creatinine level at that time was 1.9 mg/dL.

### 3. Discussion

As described by Ralli et al. [11] in the 1930s, vitamin C is excreted by the kidneys by filtration and active tubular reabsorption. The metabolism of vitamin C to oxalate was later described in the 1960s by other investigators [12, 13]. Since then, there have been several case reports in the literature mentioning acute oxalate nephropathy in association with excessive vitamin C intake. Wong et al. [19] reports a patient with metastatic carcinoma of the prostate with underlying obstructive renal insufficiency who received a 60 gm bolus of IV vitamin C as an alternative therapy and developed anuric renal failure. Two days later on renal biopsy, the patient had similar findings to our patient. Lawton et al. [14] also describes a patient with similar findings after a single administration of 45 gm of IV ascorbic acid as adjuvant therapy for primary amyloidosis with nephrotic syndrome.

In the 1970s, Sullivan and Eisenstein [15, 16] demonstrated that dialysis patients tended to lose ascorbic acid during dialysis and as a result, should receive vitamin C supplementation. Subsequently, there have been reports of cases of patients on dialysis who developed oxalate crystal deposition in various organs secondary to vitamin C supplementation [17].

Vitamin C induced acute oxalate nephropathy has also been reported in the setting of patients who received parenteral alimentation. Friedman and associates [18] describe a patient with hemolytic uremic syndrome who was given total parenteral nutrition (which included 500 mg/day of ascorbic acid) while in the hospital. The patient ended up passing away with sepsis and severe metabolic acidosis about

4 months after being admitted. An autopsy showed extensive deposition of calcium oxalate in the kidneys and pancreas. Table 1 provides a summary of the various cases reported in the literature of biopsy proven oxalate nephropathy suspected to be secondary to ascorbic acid [10, 14, 19–24].

Our patient's renal biopsy findings were similar to the biopsy findings mentioned in the cases above. Although vitamin C induced hyperoxaluria is not as common as ingestion of ethylene glycol leading to oxalate nephropathy, clinicians must consider the potential dangers of large dose ingestion of vitamin C in some individuals, especially those with underlying kidney disease or advanced age.

In conclusion, the use of vitamin C must be scrutinized closely both in patients with normal renal function and with underlying renal insufficiency. According to Auer et al. [25], "surveys have indicated that about 66% of the general public take ascorbic acid either on its own or as part of a multivitamin preparation and that ingestion of megadoses of this vitamin in excess of the recommended daily allowance is common". This figure is extremely concerning given the increasing percentage of the general public developing chronic kidney disease. We would like to add our case presentation to the literature as further evidence of this overlooked issue. Additionally, considering the improvement of our patient's condition after being treated empirically with prednisone, it is crucial to further investigate the potential benefits and improvement of prognosis with prednisone therapy in the setting of oxalate nephropathy.

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