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Editorial

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OXALATE NEPHROPATHY SECONDARY TO OXALATE-RICH DIET AND EXCESSIVE VITAMIN C INTAKE

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ABSTRACT

Oxalate nephropathy is a rare condition but remains an important cause of end-stage kidney disease. A 42-year-old man with no comorbid was referred to a nephrologist because of worsening kidney function (serum creatinine from 290 to 836 µmol/l) for the past 3 months. He was found to have impaired renal function when he was treated for pneumonia. The initial workup was unrevealing. Within a couple of weeks after the first visit, he became symptomatic with nausea and vomiting. Further history revealed that he had sought alternative treatment with numerous supplements containing high doses of vitamin C and ingesting foods with high oxalate precursor. A kidney biopsy was performed and confirmed oxalate nephropathy. Despite restriction of oxalate consumption, his kidney function deteriorated and he was initiated on long term hemodialysis.

Keywords: *Acute kidney injury, oxalate nephropathy, vitamin C*

INTRODUCTION

In the modern health-conscious world where one believes in the power of superfoods or supplements, it is not surprising that many tend to overdo with specific type of diet or harping on extra supplements for general well being. Consumption of extremely high levels of certain nutrients is detrimental to the body. We reported a case of secondary oxalate nephropathy from excessive consumption of vitamin C and oxalate-rich diet leading to the development of end stage kidney disease.

CASE REPORT

A 42-year-old Malay man with no comorbid was referred to our nephrology clinic because of worsening kidney function. He complains of nausea and vomiting for one-week duration. He had no fever, diarrhea or abdominal pain. There were no urinary symptoms or prior history of kidney stones. He had no constitutional symptoms or usage of non-steroidal anti-inflammatory drugs. He had been taking multivitamins daily for many years. He has no family history of kidney disease or kidney stones. He does not smoke or drink alcohol.

On further history, he was admitted to a district hospital two months earlier and was treated for pneumonia complicated with acute kidney injury. There were no reports of hypotensive episodes during his hospitalization. On admission, his laboratory studies showed elevated white cell counts at 19 x 103/uL, platelet of 245 x 103/uL, hemoglobin of 10.9 g/dl, urea nitrogen level of 23 mmol/L, and serum creatinine level of 552 µmol/L. Serum electrolyte results included the following values: sodium, 138 mmol/L; potassium, 4.2 mmol/L; chloride, 110 mmol/L; bicarbonate, 16 mmol/L; glucose, 8.4 mmol/L; calcium 2.2 mmol/L and phosphorus of 1.7 mmol/L. Urinalysis revealed proteinuria of 2+.

Blood cultures grew *Klebsiella pneumoniae* and he was treated with intravenous antibiotics and hydration. He responded to treatment and was discharged well with improving kidney function. Upon discharge, his urea nitrogen level improved to 14 mmol/L and serum creatinine level reduced to 310 µmol/L. Other blood parameters were within normal range. Renal ultrasound done was negative for obstruction.

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After a month of follow-up, his blood urea nitrogen was 8 mmol/L and serum creatinine of 290 µmol/. Repeat urine analysis was negative for protein, glucose or blood. Twenty-four hours urine protein reading was 0.25 gram. Further tests ruled out other causes of acute kidney injury. Autoimmune screening done showed normal C3 and C4, negative anti neutrophilic antibody (ANA), antineutrophilic cytoplasmic antibody (ANCA) panel and anti-glomerular basement membrane (anti-GBM). Uric acid, lactate dehydrogenase and iron studies were within normal range. Hepatitis panel and HIV tests were negative. A few weeks later, he developed nausea, vomiting and lethargy and was admitted to the hospital. He did not have any symptoms suggestive of infection. His vital signs were within normal range; however he looked pale and dehydrated. His laboratory tests now showed blood urea nitrogen of 25.4 mmol/l, serum creatinine of 836 µmol/l and haemoglobin 7.7 g/dL. He had metabolic acidosis with pH of 7.28 and bicarbonate of 17 mmol/l. Urine analysis sent had no traces of protein, red cells or white cells. Repeated renal ultrasound showed normal size kidneys without obstruction or stones.

He was started on intravenous hydration and hemodialysis was initiated the subsequent day as his renal function deteriorated.

A renal biopsy was done and showed the presence of 20-30% intratubular oxalate cystals, strongly birefringent under polarized light (Fig.1). There was also presence of tubular atrophy and interstitial nephritis with lymphoplasmacytic cells and eosinophils. Tubular atrophy and interstitial fibrosis were estimated at 35-40% (Fig. 2,3). These findings were consistent with acute oxalate nephropathy.

The findings on renal biopsy triggered a deeper dietary and medication history. He was on multiple types of supplements for several years and had sought for a traditional healer to improve his general health. He stopped taking animal protein and only took plant-based, high anti-oxidants meals. This included a glass of spinach juice with a handful of almonds and cashew nuts daily. He was given Vitamin C tablets 3000 mg daily amongst other supplements, both in liquid and tablet form also containing vitamin C and other minerals. All in, the amount of Vitamin C taken from the supplements was amounting up to 6000 mg daily. He was on this exclusion diet for 2 weeks.

He was treated as acute kidney injury (AKI) with acute tubular necrosis (ATN) due to oxalate nephropathy secondary to oxalate rich diet. He was advised on a low oxalate diet and to stop all the supplements. ~~Urine for 24-hour oxalate was normal.~~

As his renal biopsy reported to have features of acute interstitial nephritis (AIN), he was started on oral prednisolone 60 mg daily, tapered over a period of 4 weeks. After a few sessions of hemodialysis and strict low oxalate diet, his serum creatinine levels slowly improved. Urine for 24- hour oxalate sent one month after the ordeal was within normal range at 263 umol/day. He was then monitored in clinic. However, during clinic follow up, his serum creatinine level was creeping up gradually and by the third month his it has peaked up to 980 µmol/L with blood urea nitrogen of 29 mmol/l. He was commenced on hemodialysis.

DISCUSSION

Oxalate nephropathy is characterized by deposition of calcium oxalate crystals within the renal tubules resulting in acute and chronic tubular necrosis, interstitial fibrosis and progressive renal insufficiency. Oxalate nephropathy can be either primary or secondary (1). Primary hyperoxaluria is an autosomal recessive enzymatic deficiency that leads to increased urinary excretion of oxalate (1). In contrast, secondary hyperoxaluria occurs either due to increased dietary ingestion of oxalate or oxalate precursor (such as ethylene glycol or vitamin C), fat malabsorption from various causes (Roux-en-Y gastric bypass surgery, chronic pancreatitis and use of Orlistat) and alteration in intestinal microflora resulting in increased oxalate absorption (1).

Oxalate can be found in many foods, including peanuts, rhubarb, spinach and sweet potatoes. Intake of vitamin C rich diet or supplements has also been associated with the formation of oxalate. Recent research has indicated that with even low levels of dietary vitamin C consumption, small increases in intake (> 281 mg/day vs < 105 mg/day) in male health professionals increased kidney stone risk by 31% (2).

Several case reports have been published linking the use of vitamin C and the development of oxalate nephropathy. K. Wong et al. reported a patient with metastatic carcinoma of the prostate with underlying obstructive renal insufficiency (3). The patient received a 60,000 mg bolus of IV vitamin C as an alternative therapy and subsequently developed anuric renal failure. Renal biopsy showed oxalate nephropathy. Few cases reported excessive consumption of cashew nuts, spinach and peanuts leading to oxalate nephropathy (4-5).

Our case differs from the other reported cases as it involved oral ingestion of high dose vitamin C. The patient consumed various foods high in oxalate and multiple supplements high in vitamin C (up to 6000mg daily), above the recommended daily intake of 65-90 mg daily. Comparing with the other reports, the development of

oxalate nephropathy is not dose-dependent. Our patient's risk factors for worsening kidney function were prolonged use of supplements and recent history of AKI. He did not have any genetic conditions, bowel diseases or prior history of kidney stones.

The clinical presentation of oxalate nephropathy varies and relates more to acute kidney injury. The diagnosis is confirmed by kidney biopsy showing tubular oxalate crystals. Cases in the literature have noted various degrees of complete recovery, partial recovery and end-stage renal disease requiring life-long dialysis.

As the incidence of diet-induced oxalate nephropathy is low, specific treatment guidelines do not exist. The recommended management is a low oxalate diet, high fluid intake, and the use of calcium carbonate to bind oxalate and potassium citrate for correction of metabolic acidosis. Steroids may be given to treat the inflammatory component of calcium oxalate deposition with subsequent improvement of kidney function.

CONCLUSION

Secondary oxalate nephropathy is rare but could lead to potentially devastating condition. This case highlights the potential danger of supplementation when one doesn't fully understand the subsequent impacts on the body; it also highlights the importance of dietary history when assessing someone's health, including a diet that is too exclusive or laden with potentially harmful substances. Vitamin C taken at high doses can induce hyperoxaluric nephropathy and progressive renal failure. Renal replacement therapy is required in more than 50% of the patients studied and most patients remain dialysis-dependent.

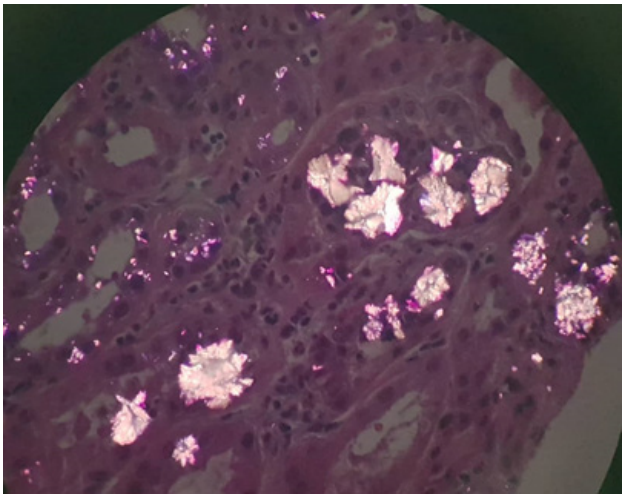

Fig. 1 Renal biopsy showing presence of intratubular oxalate crystals strongly birefringent under polarized light.

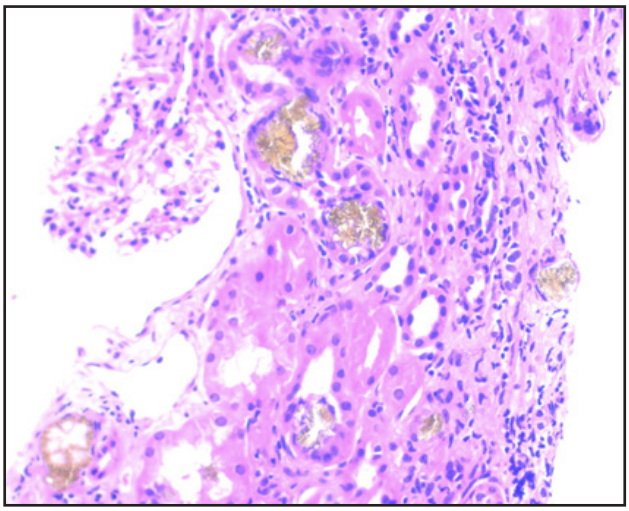

Fig. 2 Renal biopsy showing presence of tubular atrophy and interstitial nephritis (35-40%) with lymphoplasmacytic cells and eosinophils.

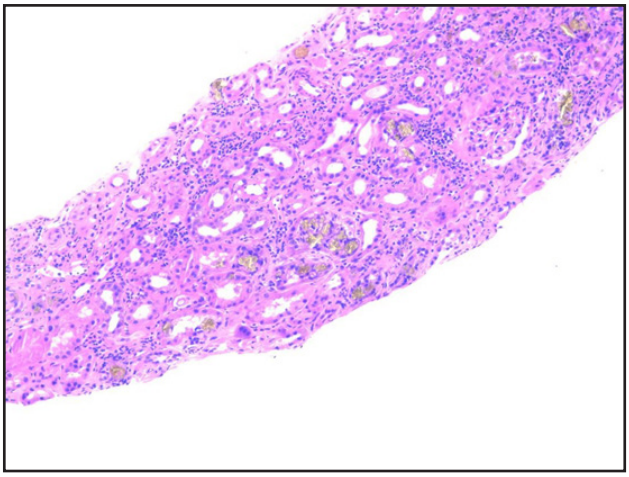

Fig.3 Renal biopsy showing presence of intratubular oxalate crystals with tubular atrophy and interstitial nephritis under H&E stain.

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