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Acute Kidney Injury after Ingestion of a Native Southeast Asian Fruit as a Complementary Remedy

A 72-year-old Indonesian male presented with nausea and vomiting 1 day after ingesting 3 bottles (total volume of 1 litre) of homemade juice from a palm-sized ovoid green fruit (Fig. 1). The sour fruit was harvested from a common native garden plant, and was recommended to him as a traditional remedy for his hypercholesterolaemia.

Fig. 1. Palm-sized ovoid green fruit

Our patient has a background of diabetes mellitus, hypertension and hyperlipidaemia. As he was not a resident in Singapore, there were no available records of baseline serum creatinine and baseline urine albumin/protein levels. Patient however claimed that he was previously told by his general practitioner in Indonesia that he did not have any renal impairment. He was not known to have ischaemic heart disease or congestive cardiac failure. His chronic medications comprised Atenolol, Fenofibrate and Gliclazide.

On admission, he did not have fever, abdominal pain, diarrhoea, gross haematuria or frothy urine. He was hypertensive with blood pressure of 181/87mmHg. Patient was alert in mentation and clinically euvolaemic –lungs were clear on auscultation and there was no peripheral oedema. Jugular venous pressure was not raised. Bladder was not palpable. Patient was not oliguric and had urine output of 800–1000ml per day.

Investigations showed a markedly elevated serum creatinine of 1146μmol/L. Urinalysis did not identify casts or microscopic haematuria. However, there was proteinuria as Urine Protein Creatinine ratio on admission was 0.80g/g. Anti-nuclear antibody, anti-dsDNA, anti-neutrophil cytoplasmic and anti-glomerular basement membrane antibodies were negative. C3 and C4 were within normal ranges. He did not have cytopenias or peripheral eosinophilia and urine eosinophils were not detected. Doppler ultrasonography of the kidneys was unremarkable. Bilateral kidneys were 10cm in length and no hydronephrosis was detected. The patient declined a kidney biopsy.

Given the above clinical presentation and the fruit presented, what is the likely cause for his acute kidney injury?

A. Sepsis
B. Pre-Renal from Gastrointestinal Losses
C. Hypertensive Emergency
D. Oxalate Nephropathy
E. Obstructive Uropathy

Clinically, patient is euvolaemic and there is no evidence of sepsis. Hence, A and B are unlikely. While the patient is hypertensive, the degree of hypertension and absence of other symptoms (especially neurological) that were suggestive of Hypertensive Emergency made the answer C unlikely. Answer E is unlikely as ultrasound imaging of the kidneys and bladder did not

Answer: D

Table 1. Trend of investigations during admission and post-discharge

Labs	Admission	D2	D4	D6	D9	1 week post-discharge	5 months post-discharge	1 year post-discharge
Urea (mmol/L)	38.1	42.0	27.1	23.6	20.8	17.4	6.2	5.8
Creatinine (μmol/L)	1101	1146	659	452	374	208	99	88
Sodium (mmol/L)	134	138	146	141	139	136	144	141
Potassium (mmol/L)	4.4	4.3	3.5	3.9	3.8	4.0	3.9	3.6
Chloride (mmol/L)	101	104	102	98	100	102	110	110
Bicarbonate (mmol/L)	15.9	15.0	26.8	27.7	25.5	23.7	24.9	26.9
Calcium (mmol/ L)	2.25					2.30	2.34	
Phosphate (mmol/L)	2.45					0.95	1.10	
Uric Acid (μmol/L)	631							
Urine Protein: Creatinine Ratio (g/g)	0.80						0.11	0.10

yield evidence for obstructive uropathy. The patient's clinical presentation after ingestion of the above fruit is consistent with D–Acute Oxalate Nephropathy. Fig. 1 shows the fruit of *Averrhoa bilimbi,* a cousin of the starfruit (*Averrhoa carambola*) and from the Oxalidaceae family. The plant is native to tropical areas such as Southeast Asia. The fruit is believed by certain communities in Southeast Asia and South Asia to improve obesity, hypertension and diabetes.[1] As undiluted juice of this fruit contains concentrated oxalic acid, ingestion can lead to elevated serum oxalate and deposition of calcium oxalate crystals in renal tubules. This damages the renal tubules and interstitium, causing acute kidney injury and over time, interstitial fibrosis.[1,2]

Acute oxalate nephropathy secondary to ingestion of *Averrhoa bilimbi* has been described in India,[1,2] but seldom in Southeast Asia. Envelope-shaped oxalate crystals were found in urine microscopy while kidney histology showed intratubular polarisable calcium oxalate crystals with acute tubular necrosis and interstitial inflammation.[1] Ultrasound of the kidneys is usually unyielding in oxalate nephropathy as seen in observational studies.[3,4] Severe acute kidney failure was not uncommon and transient renal replacement therapy was required in 60–70%,[2] but prognosis was generally good with renal recovery within 2–8 weeks.[1]

Oxalate nephropathy is uncommon and may be due to primary or secondary hyperoxaluria.[3] Primary hyperoxaluria is a rare inborn error of glyoxylate metabolism characterised by the overproduction of oxalate. Secondary hyperoxaluria is more common and is usually the result of increased oxalate intake or absorption, reduced intestinal oxalate degradation or reduced renal excretion.[3] A systematic review of secondary oxalate nephropathy between 1950 and 2018 found that enteric hyperoxaluria was the most common cause. Increased dietary oxalate intake was attributed to high-dose Vitamin C supplements, starfruit (*Averrhoa carambola*), peanuts and rhubarb.[3] Unlike the good

prognosis for acute kidney injury from *Averrhoa bilimbi*,[2] this systematic review noted that 55% required dialysis on presentation and 58% remained dialysis-dependent.

The classical history of recent ingestion of fresh concentrated *Averrhoa bilimbi* fruit juice likely led to acute kidney injury in our patient.

While inpatient, he was initiated on supportive renal replacement therapy on Day 2 of admission. Additional sessions of haemodialysis were further performed on Day 4 and 6 of admission. His renal function continued to improve without dialysis and we were able to wean him off renal replacement therapy. He was subsequently discharged and renal function was monitored closely outpatient. Table 1 shows the trend of patient's renal function, electrolytes and urine protein creatinine ratio during admission and post-discharge. Five months later, patient's creatinine levels had improved to 99µmol/L and proteinuria resolved (urine protein creatinine ratio 0.11g/g). Blood pressure was also well controlled at 124/65. No further renal replacement therapy was required.

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