Case of acute kidney injury due to bilimbi fruit ingestion
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SUMMARY
Bilimbi fruit is widely eaten in Malaysia. Rarely reported is its potential to cause acute kidney injury (AKI) in patients with prior normal renal function. The possible dangers of its consumption are still relatively unknown among many. This case highlights the importance of taking a thorough dietary history in patients with AKI. We also hope to increase awareness among healthcare professionals on the nephrotoxic and neurotoxic effects of bilimbi fruits.

BACKGROUND
Bilimbi fruit (Averrhoa bilimbi), otherwise known as ‘belimbing buluh’ in Malay and ‘tulod ulod’ in Dusun, is a popular tropical fruit. The fruit is sour and has a characteristic cylindrical shape. Bilimbi fruit can be eaten raw, cooked or pickled. Bilimbi fruit is often considered a medicinal fruit and used to treat various ailments such as cough and rheumatism. However, the fruit contains high oxalic acid levels and may become nephrotoxic when consumed in large quantities. Over the years, there have been case reports from tropical countries documenting its neurotoxicity and nephrotoxicity among patients with chronic kidney disease (CKD). Rarely reported, it may also cause acute kidney injury (AKI) in people with normal renal function. Here we present a case of AKI after the ingestion of bilimbi fruit.

CASE REPORT
A 34-year-old man who is a smoker, with no significant medical or surgical history, presented with a 5-day history of abdominal pain and diarrhoea. He has no family history of renal diseases. The colicky abdominal pain started at the left iliac fossa radiating to the back and the whole of the abdomen. One day before the onset of the abdominal pain, he consumed about 1 kg of bilimbi fruits (about 40 fruits). He was afebrile on presentation, and his blood pressure was 158 mm Hg (systolic) and 101 mm Hg (diastolic). Abdominal examination revealed mild tenderness over the lower umbilical region, and he had no pedal oedema. Cardiovascular and respiratory examinations were normal. His urine output remained good.

INVESTIGATIONS
Biochemical investigations revealed a serum creatinine of 633.89 µmol/L, potassium of 3.9 mmol/L and urea of 10.1 mmol/L. His urinalysis was normal, with no proteinuria or microscopic haematuria. Ultrasonography of his abdomen showed no evidence of obstructive uropathy. He was started on amlodipine 5 mg daily for his hypertension. Further investigations were antistreptolysin-O titre which was negative; both C3 and C4 were raised; antinuclear antibodies were negative; hepatitis B surface antigen and hepatitis antibody (anti-hepatitis C virus) were non-reactive. Since admission, his serial serum creatinine levels were in a decreasing pattern—633 µmol/L (day 1), 442 µmol/L (day 2), 401.8 µmol/L (day 3), 368.5 µmol/L (day 4), 331.3 µmol/L (day 5), 315.2 µmol/L (day 6). He was discharged on day 6 in view of his improving kidney function.

OUTCOME AND FOLLOW-UP
On outpatient review, his renal function slowly improved. Three weeks later, he reported dizziness with the amlodipine, and he stopped taking it. His blood pressure without the medication on review was 134 mm Hg (systolic) and 94 mm Hg (diastolic). His creatinine continued to improve to 169 µmol/L (day 11), 99.05 µmol/L (at 6 weeks), 107.63 µmol/L (at 10 weeks), 76.76 µmol/L (at 8 months).

DISCUSSION
Although bilimbi fruit is widely consumed in Malaysia, AKI due to Averrhoa bilimbi is rare, and case reports documenting its toxicity are scarce. Its nephrotoxicity is due to oxalate crystal deposition resulting in acute oxalate nephropathy, affecting people with normal kidney function, but more frequently in those with renal dysfunction. Bakul et al from India reported a series of cases in Kerala where 10 patients developed AKI following ingestion of bilimbi fruit juice where 7 out of 10 required haemodialysis. Nair et al also reported two cases of acute renal injury after both patients took bilimbi fruit juice as a presumed treatment for dyslipidaemia. The renal biopsy findings from patients who developed AKI following bilimbi fruit ingestion showed acute tubulointerstitial nephritis and tubular obstruction with calcium oxalate deposits. It is believed that the nephrotoxicity comes from the direct tubular damage from the calcium oxalate crystal obstruction of the tubules. Other mechanisms such as oxidative stress causing direct renal cytotoxic effects and apoptosis, indirect renal cytotoxic effects and necroinflammation from the crystals, and impairment of intracellular calcium homeostasis may also account for the severity and extent of renal damage. Consideration of other factors predisposing to AKI, such as the role of genetic and epigenetic and the effects of pre-existing comorbidities, may aid in further understanding of
the mechanisms involved in AKI secondary to dietary oxalate. Although the exact amount of bilimbi fruit ingestion (either the fruit or the fruit juice) that may cause toxicity is not determined, ingestion of a large number of fruits or its juice or ingestion on an empty stomach seems to be the risk factor. Magnesium and calcium ions in food bind to oxalate in the gastrointestinal tract, thus preventing oxalate absorption. Ingestion of bilimbi fruit on an empty stomach may result in increased oxalate absorption, leading to AKI. Some patients (such as ours here) may not require dialysis, but others may need haemodialysis or haemoperfusion. Peritoneal dialysis was reported to be ineffective in the presence of neurological manifestations.

*Averrhoa bilimbi* and *Averrhoa carambola* (starfruit) belong to the family *Oxalidaceae* and share similar biochemical properties. There are many reported cases of star fruit-induced oxalate nephrotoxicity in those with existing renal impairment. However, the oxalic acid content in star fruit is less than bilimbi (0.8–7.3 mg/g). Simon et al. reported a case of an elderly woman with CKD on dialysis who presented with intractable hiccups and altered sensorium following ingestion of both bilimbi and star fruit. The convincing time relationship between the ingestion of these fruits and the onset of symptoms in this case strongly suggests caramboxin intoxication. In 2017, Caetano et al. described the case of a patient with CKD on dialysis who developed neurological symptoms after the ingestion of bilimbi fruit, similar to those related to star fruit ingestion. Initially, it was thought the neurotoxicity was due to the high oxalate content of the fruit, but recent findings seem to suggest another neurotoxin, called caramboxin, as the responsible agent. Caramboxin is an amino acid analogue and is metabolised and excreted by the kidneys. Caramboxin has an excitatory, seizure-causing and neurodegenerative effect. The neurotoxic effects of caramboxin may be mediated by increased excitation (due to activation of NMDA, AMPA and kainate receptors) or decreased inhibition (due to decreased GABA binding). In patients with normal renal function, the neurotoxin is absorbed, distributed and excreted by the kidneys. In patients with CKD, the neurotoxin cannot be eliminated effectively by the kidneys, and its toxic effect may be fatal. The neurological symptoms of hiccups, vomiting, mental confusion, agitation and seizures in a patient with end-stage renal disease may be confused by other differential diagnoses such as uremic encephalopathy and meningencephalitis. The symptoms are known to occur within hours of ingestion; thus, a history of ingestion of the fruit may be the most crucial clue to the diagnosis in an acute setting. Caramboxin is water soluble and dialysable, and therefore intense dialysys may improve the outcome.

Despite their popularity, the potential harms of the tropical fruit bilimbi, and its close relative, the starfruit, are not well known. AKI may occur in patients with prior normal renal function following ingestion of bilimbi fruit, especially when taken in large quantity. Therefore, efforts must be made to ensure that healthcare professionals are aware of its potential neurotoxicity and nephrotoxicity. This case highlights the importance of a thorough dietary history in patients with AKI. Patients with CKD, especially those in the advanced stage, should be advised against eating bilimbi fruits.

### Learning points

- A thorough dietary history should be included in all patients with acute kidney injury.
- Healthcare professionals should be aware of the potential neurotoxic and nephrotoxic effects of bilimbi fruits.
- Patients with chronic kidney disease, especially those in the advanced stage, should be advised against eating bilimbi fruits.

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K-WW—data collection and writing the main content of the case report. MGL—editing and writing the summary, background and parts of the discussion.

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