Case Report

Acute Kidney Injury with Neurological Features: Beware of the Star Fruit and its Caramboxin

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Abstract

Star fruit (Averrhoa carambola) is a well-known product in tropical countries. There are few reports published in literature with acute kidney injury due to oxalate induced nephropathy. However, none of them have an important neurological feature. We present a case of a 51-year-old male with paresis and altered mental status. Screening for neurological diseases such as stroke, Guillain-Barre, meningitis and encephalitis were negative. In the evolution, he developed acute kidney failure and was submitted to 4 dialysis sessions. After talking to the family, we discovered he had ingested over 50 star fruits prior to the acute neurologic deficits. He recovered renal function so a renal biopsy was not required. Physicians should actively look for star fruit ingestion history in patients presenting with unexplained acute kidney injury with or without neurological features. Besides, taking star fruit in a large amount, accompanied by an empty stomach and dehydrated state, is a risk factor for neurotoxicity.

Keywords: *Acute kidney injury, Averrhoa, calcium oxalate, dialysis*

Introduction

The star fruit (Averrhoa carambola), a member of Oxalidaceae family, is popular in tropical countries as Brazil, Mexico, and India. It is a star-shaped fruit that can be classified into two categories: the sour type—richly flavored, commonly prepared as juice and with more oxalic acid; and the sweet type—mild flavored, usually consumed as fresh fruit and with less oxalic acid.[1]

It is well known the toxicity of this fruit in chronic kidney disease. If ingested, patients with renal failure can have seizures, hiccups, mental confusion, coma and even death.[2]

Formerly it was believed that patient with normal renal function could ingest the fruit without any problems. However, isolated cases in literature proved that massive ingestion of this fruit can lead to acute kidney injury and neurotoxic effects. The first one caused by the amount of oxalate and the second due to caramboxin, the neurotoxin present in the star fruit that has renal excretion.[3]

The aim of this article is to report a patient who had an acute kidney injury with neurological deficits after consuming a large number of star fruits and to perform a literature review about the same.

Case Report

A 51-year-old man presented to the Emergency Department with paresis in right side and altered consciousness. He was previously healthy and denied drug use. No alcohol or tobacco history. His vital signs were normal, afebrile, no other abnormalities in the physical examination. A computed tomography (CT) was promptly performed for stroke evaluation. Admission CT was normal, with no signs of bleeding. We did not thrombolyse the patient because he was no longer in the open window opportunity. Table 1 has other laboratory findings on admission.

At day 3 of hospitalization, he developed anuria, was tetraparetic and his creatinine value increased to 3.9 mg/dL. Another CT was performed that continued showing no acute ischemic insults. At this point, still believing in neurologic disease, the patient was submitted to lumbar puncture and magnetic resonance imaging, both without pathological findings. Herpes, Epstein-Barr, cytomegalovirus, VDRL serology, and real-time PCR for Mycobacterium tuberculosis were all negative. Even

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Table 1: Laboratory test exams at admission

Admission laboratory test	Result
Haemoglobin	14.1 g/dL
White blood cells	8490/uL
Platelet	264 000/uL
Glucose	102 mg/dL
Total bilirubin	0,3 mg/dL
Alanine transaminase	66 U/L
Aspartate transaminase	80 U/L
HIV, B and C hepatitis, VDRL	Negative
Urea	183 mg/dL
Creatinine	3.12 mg/dL
Sodium	150 mmol/L
Potassium	3.68 mmol/L
Lactate	1.3 mmol/L
Blood, urine, tracheal cultures	Negative
Lactate dehydrogenase	403 ng/dL

electromyography was performed to investigate Guillain-Barre or a myopathic disease, but it was negative as well.

Despite no signs of infection, we collected blood, urine and tracheal cultures that were all negatives. A urine exam showed more than 1 million leucocytes, 60 000 red cells, hyaline and granulose cylinders, and a 944 mg/dL protein. After this result, ceftriaxone was initiated empirically for urinary infection.

During the first week of hospitalisation he had to be dialysed four times due to hypervolemia. After dialysis initialization, we observed an improvement in his neurological deficits. A urinary ultrasound was unremarkable.

In his second hospitalization week, after a meticulous conversation with family, we discovered that he had ingested over 50 star fruits two-three days before presenting with paresis. After searching in literature, our hypothesis was that he had an acute kidney injury and neurological signs because of caramboxin intoxication. We did collect 24 h urine oxalate in the third week but it was within normal range (2.8 mg/24 h). That is probably because of the delay in sample collection (by that time he was having good urine output and renal functions were improving). A renal biopsy was not performed since the patient was having improvement. After one month the patient was discharged with no neurological deficits. His creatinine level was 2.37 mg/dL and urea 97 mg/dL. Six months after the initial event, in the nephrology outpatient clinic, his creatinine level was 1.3 mg/dL and urea 56 mg/dL.

For publication porpoise, the patient provided an informed written consent.

Discussion

There are few reported cases in the literature of star fruit toxicity [Table 2]. Notice that time since fruit ingestion and clinical presentation is highly variable, as so the amount ingested. From the published articles it can be concluded that if the patient has an empty stomach he does not need to consume a large amount of the fruit to develop the toxicity. On the other hand, a massive quantity (just like our case with 50 star fruits), independent of fasting, is a risk factor for neuro and nephrotoxicity.[2] We do not know, however, the precise maximum recommended amount of fruit or juice beyond which toxicity would be likely to appear.

Star fruit is a high source of oxalate. That explains the gastrointestinal symptoms that patients usually complain. They were not due to uremia as uremic symptom cannot develop soon after ingestion and suggest direct corrosive injury of oxalate in the digestive tract.[4]

The nephropathy induced by oxalate occurs a few hours later. The mechanism by which tubular damage occurred is the obstruction of renal tubules by these crystals as well as apoptosis of the renal tubular epithelial cells.[5]

The nephrotoxicity is strictly related to neurotoxicity. Star fruit has a neurotoxin called caramboxin, which has renal excretion and can pass through the blood-brain barrier. When renal function is abnormal there is an elevation of caramboxin in the central nervous system that results in neurological symptoms such as hiccups, paresis, seizure, coma and even death.[2,6] Moreover, there is no assay for caramboxin level yet available.

Neto *et al*.[7] had classified clinical symptoms of intoxication in uremic patients as 1) mild: hiccups (94%), vomiting (69%), and insomnia; 2) moderate: psychomotor agitation (66%), sudden-onset limb numbness, paresthesias (tingling/pricking) (41%), and muscle weakness; and 3) severe: moderate to severe mental confusion progressing to coma, seizures (22%) progressing to status epilepticus, and hemodynamic instability progressing to hypotension and shock.[7,8]

The treatment depends on clinical presentation, varying from conservative to dialysis. Some case reports used prednisolone in low doses,[9,10] urinary alkalization,[11] and diuretic therapy, all without a good evidence level.[12] Dialysis, on the contrary, seems the most reasonable treatment especially when neurological symptoms are present, since it is believed that caramboxin is dialyzable and may increase oxalate clearance, apart from the removal of uremic toxins.[2,10] However, there are no studies describing the use of hemodialysis for the sake of removal of oxalate *per se* without any other nephrological indications. We think that earlier dialysis can be performed if star fruit intoxication is hypothesized, especially with a disturbance in the conscious level or other neurological feature (peritoneal dialysis has been shown to be of no benefit, especially in these type of patients).[10,13,14] In our case, after initiation of dialysis sessions patients paresis improved. Dialysis could be started

Table 2: Review of case reports with acute renal failure due to star fruit ingestion

Author and year	Patient	Details of fruit ingestion	Clinical manifestation and time after star fruit ingestion	Basal creatinine	Time for complete renal recovery and creatinine value	Histopathology	Urinary analysis	Dialysis	Comment
Present case	Male, 51 years	50 star fruits	Acute renal failure and paresis; 2-3 day	Not reported; 3.12 mg/dL at admission	6 months; 1.3 mg/dL	Not performed	Leukocyturia, proteinuria and hematuria	Yes, 4 sessions	First report with a remarkable neurological finding
Molina[11] *et al.*, 2016	Female, 55 year	2-3 glasses in fasting	Bilateral lumbar pain, nausea, asthenia; 2 h	Not informed; 4.55 mg/dL at admission	3 weeks; 1.4 mg/dL	Not performed	Urate crystals	No	Treated with urinary alkalization with potassium citrate
Su YJ[14] *et al.*, 2011	Female, 63 years	1000 mL of pure fruit juice on an empty stomach	Oliguria and leg edema; 5 days	Not informed; 6 mg/dL at admission	1 month; 0.9 mg/dL	Oxalate nephropathy	Proteinuria and hematuria	No	-
Chen[13] *et al.*, 2001	Male, 77 year	1600 mL of pure sour juice on empty stomach	Nausea, vomiting, lower back pain; within hours	Not informed; 51 mg/dL four days after star fruit ingestion	28 days; 1.5 mg/dL	Oxalate nephropathy	Hematuria	Yes, 2 sessions	First case report published
	Male, 38 years	3,000 mL of undiluted sour carambola juice on empty stomach	Abdominal pain and backache; 4 hours	Not informed, 1.6 mg/dL at admission	28 days; 1.5 mg/dL	Oxalate nephropathy and IgA deposition in the mesangium	Hematuria, proteinuria and leukocyturia	Yes, 5 sessions	
Scaranello[6] *et al.*, 2014	Female, 44 years	Juice with 20 carambolas and ingested more 30 fruits	Diarrhea, nausea, vomiting, oliguria and abdominal pain; 1 day	0.8 mg/dL; 9 mg/dL at admission	10 days; 1.1 mg/dL	Not performed	Hematuria, proteinuria, leukocyturia and oxalate crystals	Yes, 2 sessions	Report with most precocious renal recovery
Neto[3] *et al.*, 2009	Male, 48 years	15 fruits on empty stomach	Hiccups; 7 h	0.89 mg/dL	Not informed; 1.1 mg/dL	Not performed	Not available	No	-
	Male, 49 years	1000 mL of pure juice	Hiccups, vomiting, insomnia; 3 h	0.9 mg/dL; peak during hospitalization 6.2 mg/dL	Not informed; 1.1 mg/dL	Not performed	Hematuria	No	
	Female, 67 years	1500 mL of pure juice	Hiccups, vomiting, diarrhea, back pain, mental confusion; 3 h	1.2 mg/dL; peak during hospitalization 6 mg/dL	Not informed; 1.2 mg/dL	Not performed	Leukocyturia and oxalate crystals	No	
	Male, 66 years	300 mL of pure juice, empty stomach	Hiccups, vomiting, back pain; half hour	1 mg/dL; peak during hospitalization 5.6 mg/dL	Not informed; 1 mg/dL	Oxalate nephropathy	Oxalate crystals	No	
	Male, 34 years	12 fruits, empty stomach	Back pain, nausea, insomnia; 1 h	1.1 mg/dL; peak during hospitalization 4 mg/dL	Not informed; 1.1 mg/dL	Oxalate nephropathy	Oxalate crystals	No	
Abeysekera[9] *et al.*, 2015	Female, 56 years	200 mL of concentrated juice of six star fruits	Generalized weakness and lethargy; 12 days	0.9 mg/dL; 3.28 mg/dL at admission	3 weeks; 0.96 mg/dL	Oxalate nephropathy	Proteinuria and leukocyturia	No	Given oral prednisolone due to the presence of interstitial nephritis

Contd...

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Author and year	Patient	Details of fruit ingestion	Clinical manifestation and time after star fruit ingestion	Basal creatinine	Time for complete renal recovery and creatinine value	Histopathology	Urinary analysis	Dialysis	Comment
Barman[4] *et al.*, 2016	Male, 30 years	10 fruits, 500 mL juice, empty stomach	Abdominal pain, oliguria; 6-10 h	Not informed; 23.7 mg/dL at admission	Not informed	Acute tubular necrosis	Proteinuria and hematuria	Yes, number not available	Case series with more young patients
	Male, 29 years	1000 mL juice	Abdominal pain, oliguria; 12-15 h	Not informed; 17.1 mg/dL at admission	Not informed	Acute tubular necrosis and oxalate nephropathy	Proteinuria	Yes, number not available	
	Male, 45 years	5-6 fruits, 500 mL juice	Back pain, nausea, oliguria; 10-12 h	Not informed; 6 mg/dL at admission	Not informed	Acute tubular necrosis and oxalate nephropathy	Proteinuria	No	
	Male, 20 years	6-8 fruits, empty stomach	Nausea, oliguria; 10-14 h	Not informed; 11.7 mg/dL at admission	Not informed	Acute tubular necrosis	Proteinuria	Yes, number not available	
	Female, 15 years	4-6 fruits	Hiccups, abdominal pain; 28-30 h	Not informed; 3.2 mg/dL at admission	Not informed	Not performed	Proteinuria	No	
Wijayaratne [10] *et al.*, 2017	Male, 52 years	200 mL of homemade star fruit juice made from four whole star fruits	Loose stool, abdominal pain, oliguria; few hours	0.7 mg/dL; 4.5 mg/dL at admission	3 months; not informed	Oxalate nephropathy	Nothing remarkable	Yes, 1 session	-
	Male, 65 years	3 star fruits	Poor appetite, poor sleep, nausea and dyspeptic symptoms; not informed	1.2 mg/dL; 7.3 mg/dL at admission	10 months; 1.4 mg/dL	Acute tubule-interstitial nephritis	Nothing remarkable	No	Given prednisolone 30 mg daily
	Male, 57 years	One star fruit daily over the preceding one year with increased consumption to 3 fruits per day over the preceding one month	Loss of appetite, nausea, diarrhea; consuming daily 3 fruits for the past month	Not informed; 13.16 mg/dL at admission	2 months; 2.98 mg/dL	Oxalate nephropathy occurring in the background of early diabetic nephropathy	Hematuria and leukocyturia	Yes, number not informed	Given prednisolone 30 mg daily

sooner even without classic indications due to severe neurological impairment, but star fruit intoxication was not one of our firsts differentials diagnosis.

Recently the effect of N-acetylcysteine on star fruit induced acute kidney injury was studied in animal models. The results suggest that this drug can reduce oxidative stress, oxaluria, and inflammation, attenuating renal dysfunction in the final analysis.[1] It is important to emphasize that acute events related to star fruit intoxication have a good prognosis. Every case reported in the literature had a recovery in renal function and no deaths. In chronic kidney disease, however, death can occur in 61% and 42% of patients with seizure and confusion, respectively.[2]

Conclusion

To the best of author's knowledge, there is no report in literature with such important neurological feature in acute star fruit intoxication. Our diagnosis was delayed because we believed in neurological disease. The decrease in renal function helped to seek of other differentials, but the strong epidemiology of star fruit consume closed the diagnosis and no biopsy was needed. Therefore, every patient presenting with acute kidney failure with or without neurological features should be questioned about star fruit consume. Physicians should guide patients not to ingest a large amount of star fruit, especially on an empty stomach or in a dehydrated state.

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Conflicts of interest

There are no conflicts of interest.

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