



Case report

Starfruit neurotoxicity mimicking an acute brainstem stroke

Frederico Fernandes Alessio-Alves^a, Carolina Pinto de Souza^a, Luciana Karla da Silva^a, Miguel Moyses-Neto^b, Octávio Marques Pontes-Neto^{a,*}

^a Department of Neurosciences and Behavioural Sciences, Ribeirão Preto School of Medicine, University of São Paulo, Ribeirão Preto, Brazil

^b Division of Nephrology, Department of Internal Medicine, Ribeirão Preto School of Medicine, University of São Paulo, Ribeirão Preto, Brazil

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1. Introduction

The carambola (*Averrhoa carambola*), also known as the starfruit, is originally native to Southeastern Asian countries, such as the Philippines, Indonesia, and Sri Lanka. About 150 years ago, it was brought to the western land, including Brazil, where its juice is used as a diuretic, expectorant, and cough medicine. There have been reports of patients with chronic renal failure who developed neurological alterations associated with the ingestion of this fruit. It is believed that Carambola contains neurotoxins that are usually excreted by the kidneys and may accumulate in patients with renal insufficiency. Those toxins are thought to overcome the blood–brain barrier giving rise to a variety of presentations—from persistent hiccups to status epilepticus and coma [1], which, thus, can be misinterpreted as a stroke. Herein, we report a case admitted at our Emergency Department with a stroke-like episode caused by starfruit toxicity.

2. Case report

A 52-year-old male patient with high blood pressure under chronic hemodialysis associated with renal polycystic disease was admitted at the Emergency Unit of the University Hospital of

Ribeirão Preto School of Medicine, University of São Paulo. He presented with a sudden burst of hiccups, elevated blood pressure, convulsions, and confusion. The neurological examination consisted of altered mental status (Glasgow Coma Scale of 13), bilateral ophthalmoparesis, left facial central paresis, and severe ataxia. These focal signs further progressed and tetraparesis and loss of gag reflex were observed and initially interpreted as a possible brainstem vascular ailment. Furthermore, pupils were equal and round, reactive to light and accommodation (direct and consensual), corneal reflex was present bilaterally, plantar response was indifferent, and no clonus was observed. There was no tremor, myoclonus, asterix or tetany. The non-contrast CT had no signs of brain hemorrhage and thrombolytic treatment with rTPA was considered. A non-convulsive status epilepticus was also considered and he was started on phenytoin without improvement. The laboratory screening revealed a plasma creatinine of 10.8 mg/dL and urea of 209 mg/dL, along with severe metabolic acidosis (pH = 6.84 and bicarbonate 6 mmol/L). He was then taken to urgent hemodialysis. After eighteen hours symptoms improved dramatically and neurological exam became completely normal. Once awake, he reported ingestion of a large amount of starfruit twelve hours prior to the onset of symptoms. A MRI study was subsequently acquired and revealed only asymptomatic chronic small vessel disease, without any signs of acute cerebral ischemia.

3. Discussion

The ingestion of starfruit has been related to central nervous system toxicity since 1980. A neuroexcitatory toxin was initially postulated, when normal mice were injected with carambola

* Corresponding author at: Departamento de Neurociências e Ciências do Comportamento, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Av. dos Bandeirantes 3900, Ribeirão Preto, SP CEP 14049-900, Brazil.
Tel.: +55 16 3602 2548; fax: +55 16 3602 2548.

E-mail address: opontesneto@fmrp.usp.br (O.M. Pontes-Neto).

extract in the peritoneal cavity and developed convulsions [2]. Subsequently, some authors have proposed oxalate as responsible for such effect. In fact, each fruit contains a high amount of oxalate, a substance presumably linked to encephalitis in patients receiving sugar surrogates in intensive care units [3]. Oxalate is essentially excreted by the kidneys, and impaired renal function seems to be a critical factor for the toxicity. Nevertheless, the presence of an additional neurotoxin is still controversial [3].

To our knowledge, this is the first report that starfruit toxicity may present with symptoms and signs that mimic an acute brainstem stroke, such as ophthalmoparesis, central facial paresis, loss of gag reflex, tetraparesis and coma. Intractable hiccups, the first complaint of our patient, are well described as the most common symptom related to the starfruit toxicity. A grading system was proposed based on clinical findings, from mild (hiccups, vomiting, insomnia); moderate (agitation, distal paresthesia); to severe toxicity (convulsions, status epilepticus and hemodynamic instability). In severe cases, sudden onset of focal neurological signs has also been reported [1].

The acute management of severe starfruit toxicity is still debated [4]. Urgent hemodialysis seems to be necessary, but does not always reverse the clinical picture. Our patient had a complete recovery with hemodialysis that was done in the first three hours after admission. Anti-epileptic medications are recommended for the management of status epilepticus related to starfruit toxicity. One report indicates that propofol provides better results than phenytoin, benzodiazepines and phenobarbital, what has been attributed to a faster onset of action and its predominant hepatic metabolism [4]. Our patient was not diagnosed with status epilepticus, but had a mental status impairment, and recovered before an electroencephalogram could be done.

The complete recovery after hemodialysis in a patient with high blood pressure and chronic renal failure may also be related to improvement of a uremic encephalopathy. Such cases can present with complex mental changes, confusion, delirium, psychosis, motor disturbances (tremor, myoclonus, asterixis), hyperreflexia, and disturbances of gait and speech—which are more commonly settled on chronic rather than acute failures [5]. Nevertheless, ophthalmoparesis and asymmetric cranial nerve palsies are not common in this setting. Indeed, it is very unlikely that focal brainstem findings that showed rapid improvement with hemodialysis could be attributed to an acute uremic encephalopathy only.

Until now, the diagnosis of starfruit toxicity cannot be made through a specific laboratory exam. A non-contrast CT, commonly chosen to avoid additional nephrotoxicity, is usually normal even in

severe starfruit toxicity. In a recent report, MRI of five patients with severe toxicity revealed lesions with low signal on apparent diffusion coefficient and increased signal on DWI. Those lesions were diffusely and bilaterally distributed over the cerebral cortex in one patient. In the other four, they were focally distributed over the cerebral cortex, thalami (pulvinar nuclei) and hippocampi. Authors discuss that these characteristics can be found in ischemic stroke lesions, but also in several other conditions such as anoxia, Wallerian degeneration, status epilepticus, diffuse axonal lesions and Creutzfeldt–Jakob disease [6].

4. Conclusion

Starfruit toxicity may mimic stroke in patients with chronic renal failure. Uremic patients must be alerted about the risk of neurotoxicity where starfruit is commonly consumed. Emergency staff should be aware about this condition to ensure accurate diagnosis and avoid consequences of inappropriate treatment. Starfruit toxicity has a high mortality rate related to status epilepticus and hemodynamic instability, and rapid management with hemodialysis and anti-epileptic drugs remain the mainstream of the treatment. Future studies are important to further explore the pathophysiology of the neurotoxic effect in order to allow a more specific treatment.

Disclosures

Authors disclose no conflict of interest regarding this study. Authors would like to acknowledge and thank Dr. Matt Siket for his review of the manuscript.

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