Star fruit intoxication in a chronic renal failure patient: case report

Intoxicação por carambola em paciente com insuficiência renal crônica: relato de caso

ABSTRACT

Chronic renal failure is a high morbidity and mortality condition, with its terminal phase incidence and prevalence steadily growing year after year. According to the Sociedade Brasileira de Nefrologia [Brazilian Society of Nephrology], the main causes of renal failure are arterial hypertension, glomerulonephritis and diabetes mellitus. Several factors are implied in chronic renal failure patients’ risk of mortality, particularly age, diabetes and associated co-morbidities. For patients below 50 years old, the 5 years survival rate is 62% and for those above this age and with diabetes mellitus, just 23%. Star fruit is native from Asia, and widespread in tropical countries; this fruit was reported as having a neurotoxin able to cause serious neurological changes in chronic renal disease patients. These may range from mild features, such as hiccup and confusion, to serious episodes with seizures and death. This neurotoxin apparently inhibits specifically the GABAergic conduction system. This paper describes a case involving a chronic renal disease patient who, after ingesting star fruit, featured malaise, nausea and vomiting, followed by repeated convulsions and died even though undergoing conventional hemodialysis therapy.

Keywords: Renal insufficiency, chronic/complications; Plant poisoning/complications; Neurotoxins/adverse effects; Case reports

INTRODUCTION

Chronic renal failure (CRF) is defined as increased urinary protein levels (> 150 mg/day) and/or reduced glomerular filtration rate (< 60 mL/min) for more than three months. Chronic renal failure is a high morbidity and mortality condition, and this disease incidence and prevalence steadily grow year after year. According to the Sociedade Brasileira de Nefrologia [Brazilian Society of Nephrology], the main CRF causes are arterial hypertension, glomerulonephritis and diabetes mellitus. It is not precisely known how many patients in Brazil have some degree of renal function impairment, however arterial hypertension is estimated to involve at least 25% of the Brazilian adult population. No more than 15% of these hypertensive patients have their arterial blood pressure appropriately controlled; therefore, the remainder have a potential to develop CRF. To these figures we could add the diabetes prevalence (about 7.5% of the adult population), and potentially 30% of them developing CRF. Regarding the CRF progression,
several factors increase the risk of death, mainly age, diabetes and associated co-morbidities. For patients under 50 years old, the 5 years survival rate is 62%, and for those above 50 years old and with diabetes mellitus, only 23%.[1]

Star fruit belongs to the Oxalidaceae family, species Averrhoa carambola. It is believed to be natural from Sri-Lanka, cultivated in Asian Southeast and Malaysia for centuries, and acclimatized to several tropical countries, including Brazil. This fruit has two main types, the sourer one with higher oxalic acid contents and the sweeter containing less oxalic acid.

Star fruit, widespread in tropical countries, was reported to have a neurotoxin able to cause serious neurological changes in chronic renal disease patients. These can range from mild features such as hiccup and mental confusion to serious cases with seizures and death. This neurotoxin appears to inhibit specifically the GABAergic conduction system.[2]

Star fruit intoxication was first described in 1980 by Munir and Lam,[3] in Malaysia, where the fruit was observed to cause central nervous system depressive effect. Although almost 30 years elapsed since the first description, no consensus is so far available on the responsible toxin for the star fruit effects on the central nervous system nature. Neto et al.[4] emphasized the correlation between star fruit and tonic-clonic seizures induction. In 2001 Chen et al.[5] and Fang et al.[6] correlated the star fruit’s high oxalate level with development of acute nephropathy in rats, and more recently, Fang et al.[7] in a 2007 study have shown the oxalate important role on the star fruit toxicity, inducing mioclonus and tonic-clonic seizures in nephrectomized rats fed with star fruit extract.

As the nature of the neurological changes, the treatment of star fruit intoxication is so far not well established. Hemodialysis is known to be a good option, and peritoneal dialysis should not be prescribed, due to unsatisfactory outcomes. The greatest dilemma involves choosing the hemodialysis type. Chan et al.[8], in their study published in 2009, presented three patients whose symptoms worsened following conventional hemodialysis, and who promptly responded to 8 hours activated charcoal hemodialysis sessions.

This paper aims to report a case involving a chronic renal disease patient after star fruit ingestion. Star fruit intoxication particularities are discussed, highlighting the need to warn chronic renal disease patients to avoid star fruit ingestion.

CASE REPORT

This case involved a 56 years old male patient, who was both hypertensive and diabetic, and was diagnosed chronic renal failure but still not requiring dialysis. Two days before the hospital admission he ingested four star fruits in a day. About 24 hours after the ingestion he complained of malaise and headache associated with nausea and vomiting.

The next morning, having no improvement after use of symptomatic medicines at home, the patient had three consecutive generalized tonic-clonic seizure episodes, followed by reduced consciousness level. By admission at Hospital Metropolitano/Butantá – SP he was confused, made little contact and had a Glasgow coma scale of 10. His heart rhythm was regular and heart sounds were normal. Blood pressure was 110 x 60 mmHg.

Upon admission his laboratory tests results were: blood count: hemoglobin 12.6 g/dL, hematocrit 34.2%, white blood cells (WBC) 9,200/mm³, and platelets 260,000/mm³. Serum sodium level was 145 mEq/L, potassium 4.7 mEq/L, blood urea nitrogen (BUN) 102 mg/dL and creatinine 1.8 mg/dL (the last two, increased).

Cerebrospinal fluid collected by lumbar puncture was clear, colorless, with no red blood or neoplastic cells, normal glucose, white blood cells and urea. Bacteria, latex and China ink tests were negative.

Admission head computed tomography showed no change.

The patient was medicated with Hydantal and referred to the intensive care unit (ICU) for urgent hemodialysis; however, before it could be started he featured a new convulsive crisis, and progressed with worsened consciousness level, and the Glasgow coma scale changed to 6. He was intubated, and progressed with hypotension not responsive to volume replacement; therefore vasoactive drug therapy was started with noradrenaline. After stabilization, the first hemodialysis cycle was started.

After three days in the ICU and daily hemodialysis, he remained vasoactive drug-dependent, needing progressively higher doses. Routine laboratory tests showed hemoglobin 11.3 g/dL, hematocrit 33.8%, WBC 18,300/mm³, platelets 273,000/mm³. Serum sodium was 144 mEq/L, potassium 6.0 mEq/L, BUN 136 mg/dL, creatinine 4.9 mg/dL. The patient presented significant bradycardia with hemodynamical instability, not responsive to drug therapy. The electrocardiogram...
showed junctional rhythm bradycardia, and a trans-venous pacemaker was implanted, with hemodynamical improvement. However, this improvement was transitory, and the patient died during the first hours of the fourth day after his admission to the hospital.

**DISCUSSION**

We described a case involving a chronic renal failure 56 years old male patient, who after eating star fruit had reduced consciousness level and recurrent convulsive crises. Conventional hemodialysis therapy was started with no clinical improvement, and the patient died four days after the fruit ingestion.

Hiccup is the most frequent symptom of star fruit intoxication (see Chart 1), and is usually unresponsive to conventional therapies. Seizure crises are an important prognosis factor, related to about 75% mortality. Without seizures, the mortality is about 0.03%.(9)

**Chart 1 – Star fruit intoxication symptoms**

<table>
<thead>
<tr>
<th>Intoxication level</th>
<th>Signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Hiccup, vomiting, insomnia</td>
</tr>
<tr>
<td>Moderate</td>
<td>Agitation, numbing, paresthesias, and strength loss, mild mental confusion</td>
</tr>
<tr>
<td>Severe</td>
<td>Serious mental confusion and coma, seizures and status epilepticus, hemodynamical instability with hypotension and shock</td>
</tr>
</tbody>
</table>

In kidney disease free subjects the star fruit neurotoxin is absorbed, distributed and renally excreted, entailing no disorders; however in renally impaired patients, the toxin is not appropriately excreted, with its serum levels building up, allowing the blood-brain barrier to be crossed and the consequent central nervous system effects. Some studies show that the neurotoxicity comes from the oxalate. In animal studies, Chen et al.(5) and Fang et al. (6,7) reproduced the star fruit intoxicated patients’ neurological changes in nephrectomized rats fed with star fruit extract. In this study the oxalate role was highlighted for the findings that rats fed with oxalate-free star fruit extract didn’t feature the neurological changes.

In a trial conducted by the Faculdade de Medicina de Ribeirão Preto, a star fruit neurotoxin (AcFx) was identified as acting by direct GABAergic system inhibition. Its chemical characterization showed a non-proteic molecule, with a molecular weight below 500 (about 250 daltons), which is different from oxalate.(2)

Regarding therapy, dialysis therapy is known to be the best option, however its modality, duration and number of sessions are still controversial, and so is the best starting time.(10) In a retrospective trial Chang et al.(11) identified that among 20 patients, eight died even after emergency dialysis; however, two pieces of information are not clear: the total dialysis time and the time from the intoxication to the therapy start. Daily dialysis, with 5 to 10 hours duration appears to be the best therapy option, and in worse cases, continued dialysis has improved results, especially because rebound is common. We remind that peritoneal dialysis is not effective for these cases, probably due to the neurotoxin molecular weight. Wu et al. (10) reported on two patients treated with activated charcoal hemodialysis with excellent response to therapy, quickly recovering their consciousness levels and significantly reduced intensive care stay.

In our literature review we found reports of patients with worsened neurological status following conventional hemodialysis, (8) and also that star fruit intoxication may be equally serious in chronic dialysis patients and chronic conservative therapy patients.

**CONCLUSION**

We report on a star fruit intoxication case involving a 56 years renal disease male patient who failed to respond to conventional dialysis therapy, and died 4 days after the fruit ingestion.

This case illustrates the difficulty to explain the actual intoxication cause, its symptoms severity and the still unsolved therapy uncertainties.

Importantly, one should warn our chronic renal disease patients, either those under conservative or dialysis therapy, to do not eat star fruit. This should be the responsibility of the entire health care team involved in renal disease patients’ care.

**RESUMO**

A insuficiência renal crônica é doença de elevada morbidade e mortalidade e sua incidência e prevalência em estágio terminal têm aumentado progressivamente a cada ano. Segundo a Sociedade Brasileira de Nefrologia, as principais causas de insuficiência renal crônica são hipertensão arterial, glomerulonefrite e diabetes mellitus. Diversos fatores elevam o risco de mortalidade em pacientes com nefropatia crônica, principalmente idade, presença de diabetes e número de co-
morbidades associadas. Para pacientes com menos de 50 anos de idade a taxa de sobrevida em 5 anos é de 62% e para aqueles acima desta idade e com diagnóstico de diabetes mellitus a sobrevida é de apenas 23%. A carambola, fruta originária da Ásia e muito difundida na maioria dos países tropicais, tem sido reportada como contendo uma neurotoxina capaz de provocar graves alterações neurológicas em pacientes com histórico de nefropatia crônica. Dentre estas alterações podemos observar desde quadros leves, como soluços e confusão mental, até quadros mais sérios, como convulsões e morte.

Essa neurotoxina parece apresentar especificamente inibição sobre o sistema de condução GABAérgico. Descrevemos o caso de um paciente nefropata crônico que, após ingestão de carambola, iniciou quadro de mal-estar, náuseas e vômitos, seguidos de episódios convulsivos reentrantes e vai a óbito mesmo com o tratamento hemodialítico convencional.

Descritores: Insuficiência renal crônica/complicações; Intoxicação por plantas/complicações; Neurotoxinas/efeitos adversos; Relatos de casos

REFERENCES


Rev Bras Ter Intensiva. 2010; 22(4):395-398