Star Fruit Intoxication in a Patient with Moderate Renal Insufficiency Presents as a Posterior Reversible Encephalopathy Syndrome

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Abstract-

Purpose: Star fruit has been reported to contain neurotoxins that often cause severe neurological complications in patients with uremia or severe chronic renal insufficiency. However, the occurrence of neurotoxicity in patients with mild or moderate renal insufficiency has rarely been mentioned.

Case report: A 67-year-old woman who had diabetes mellitus and moderate renal insufficiency presented with acute onset of hiccups and nausea two hours after ingestion of one fresh star fruit. She further presented with progressively incoherent speech, echolalia and bizarre behavior. On the next day, her consciousness level declined to deep coma and she experienced two seizures. Brain magnetic resonance imaging examinations revealed a focal cerebral lesion over the left occipital area. The clinical symptoms recovered and the brain lesion reversed after emergency hemodialysis.

Conclusion: The clinicians should be aware that star fruit intoxication must be considered when patients with a chronic renal disease, even mild or moderate chronic renal insufficiency, present with unexplained neurological or psychiatric symptoms. Emergency hemodialysis or other replacement therapies may be required for the management of acute star fruit intoxication.

Key Words: star fruit intoxication, neurotoxin, seizure, hemodialysis

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INTRODUCTION

Star fruit (Averrhoa carambola), originating from the Southeastern Asia in prehistoric times, is cultivated in many tropical and warm subtropical areas including Taiwan, Brazil, Thailand, Malaysia, Indonesia, India and Southern China [(1)]. In Taiwan, this popular fruit is usually consumed fresh, pickled or as juice. Star fruit is also recommended as a diuretic or as an expectorant and cough suppressant [(2)].

Star fruit has been reported to contain neurotoxins that often cause severe neurological complications in patients with uremia or severe chronic renal insufficiency[(2,3)]. The most common symptoms in star fruit intoxi-

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cation include persistent and intractable hiccups, vomiting, variable degrees of disturbed consciousness, psychiatric symptoms, decreased muscle power, paresthesia, paresis, insomnia, seizures and death[2-4]. The mortality rate after star fruit intoxication ranges as high as 20% to 40%[2,3]. Seizures, particularly status epilepticus, have been proposed to be associated with poor prognosis and high mortality rate[4]. Whereas star fruit intoxications have been reported mainly in uremic patients[2,3], the occurrence of neurotoxicity in the patients with mild or moderate renal insufficiency has rarely been mentioned[5]. Herein, we report a case of star fruit intoxication associated with moderate renal insufficiency. In this patient, brain magnetic resonance imaging (MRI) examinations revealed a reversible focal cerebral lesion over the left occipital area. The clinical symptoms recovered and the brain lesion resolved after emergency hemodialysis.

CASE REPORT

A 67-year-old woman was admitted to our neurologic intensive care unit due to acute onset of consciousness disturbance. She had underlying type 2 diabetes mellitus with mild chronic renal insufficiency (serum creatinine, 1.45 mg/dL) under regular oral hypoglycemic agent treatment. There was no history of alcohol or drug addition, other systemic diseases or psychiatric disorders. In the morning of the day before admission, she suffered from acute onset of hiccups and nausea two hours after ingestion of one fresh star fruit. Her consciousness level declined gradually during the day. She began to have incoherent speech, echolalia and bizarre behavior in the evening. In the next morning, she was sent to our emergency room with a deep comatose state on arrival. Her blood pressure was 132/75 mmHg, heart rate 72 beats/min, and body temperature 37.1 ˚C. Initial neurological examination revealed bilateral isocoric pupils with a preserved light reflex. Initial laboratory investigation revealed that her glucose level was 490 mg/dL (70-105), blood osmolarity 317 mmol/kg (275-295), blood urea nitrogen (BUN) 30 mg/dL (7-20) , serum creatinine 1.89 mg/dL (0.44-1.03) , sodium 141 mmol/L (134-148), potassium 3.1 mmol/L (3.0-4.8), ammonia 28 μmol/L (< 94), and white blood cell count 22×10^9/L (3.5-11). A cerebrospinal fluid examination was normal. Other laboratory tests for drug screening, aspartate transaminase, alanine transaminase, syphilis, antinuclear

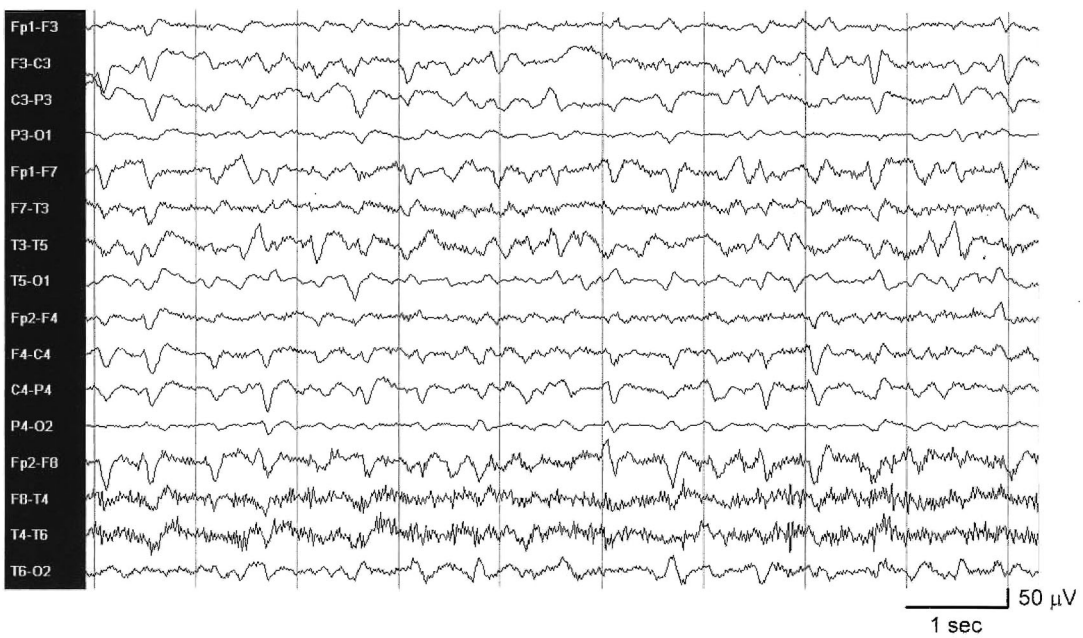

Figure 1. An EEG shows slowing of background with diffused triphasic waves.

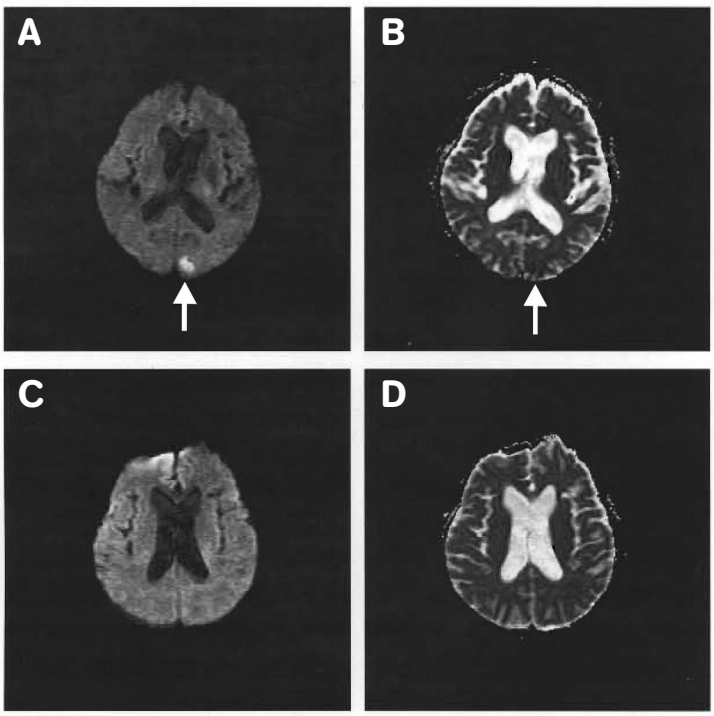

Figure 2. During the acute stage of star fruit intoxication, axial views of brain magnetic resonance imaging (MRI) diffusion-weighted images (DWI) (A) shows a hyperintensity lesion (arrow) in the left occipital lobe with a corresponding hypointensity signal (arrow) in apparent diffusion coefficient (ADC) (B). Two weeks after intoxication, as the patient regained full consciousness, the cytotoxic edema had completely resolved on the corresponding DWI (C) and ADC (D).

antibody, tumor markers, thyroid function and cortisol level were unremarkable. Electrocardiography and a chest X-ray revealed normal results. No bacteria were yielded from the blood cultures. Electroencephalogram (EEG) showed diffuse slowing of the background and presence of triphasic waves (Fig. 1). Brain MRI revealed a focal hyperintensity on diffusion-weighted imaging (DWI), with a corresponding hypointensity signal of apparent diffusion coefficient (ADC) in the left occipital region (Fig. 2A, B).

After admission to the intensive care unit, she experienced two seizures with left mouth angle twitching and left upper limb clonic convulsions. The seizures were controlled by intravenous valporate therapy. Under the impression of star fruit intoxication, emergency hemodialysis was performed. After hemodialysis, the patient gradually regained consciousness. A repeated brain MRI two weeks after a session of hemodialysis showed that the lesion had completely resolved (Fig. 2C, D). EEG conducted on the same day also showed improvement of the background. The patient was discharged two weeks later without neurologic sequelae.

DISCUSSION

Patients with chronic renal insufficiency are vulnerable to developing intoxication through drugs or toxins, and star fruit is probably the only natural fruit that is associated with neurotoxicity in such patients [6]. The first report of star fruit neurotoxicity appeared in 1980 [7], with star fruit extract injected intraperitoneally into normal mice, resulting in convulsions. Moreover, an intracerebroventricular injection of the fruit extract in rats or mice induces immediate and persistent tonic-clonic convulsions [3]. It has been postulated that an excitatory neurotoxin of an unknown nature exists in star fruit, which could be responsible for the neurological complications in patients with chronic renal disease.

Our patient exhibited the manifestations of star fruit intoxication, which included hiccups, nausea and vomiting, behavior changes, disturbed consciousness, decreased muscle power, and seizures. The diagnosis of star fruit intoxication is supported by a close temporal relationship between the time of star fruit ingestion and development of the symptoms. However, known etiolog-

ic conditions causing acute consciousness disturbance, such as toxins, drugs, alcohol, trauma, cerebral vascular insults, central nervous system infections, hepatic or renal encephalopathy and hypoxia, could not be found in our patient. Lack of infectious signs and fever and the negative blood cultures essentially excluded the sepsis as the cause for leukocytosis. Therefore, we proposed that the leukocytosis and hyperglycemia may be secondarily provoked by the star fruit intoxication in this patient. In addition, an interictal EEG revealed a diffuse slowing background and diffuse triphasic waves that may suggest an encephalopathy caused by star fruit intoxication.

The renal insufficiency in this case was less severe than in reported cases. The estimated creatinine clearance for this patient by the Cockcroft-Gault formula was 31.9 mL/min, and the degree of renal impairment was moderate. Star fruit intoxications have been reported mainly in patients with uremia or severe chronic renal insufficiency [2,3]. However, severe star fruit intoxication can also occur in patients with moderate chronic renal insufficiency and eventually developing a potentially fatal outcome [5]. The pathophysiologic mechanism of the neurotoxicity of star fruit in chronic renal insufficiency still remains unclear. In patients with mild or moderate renal insufficiency, it has been proposed that the dehydrated state contributes to the neurotoxicity [5]. The high coincidence of diuretic use in the patients with renal insufficiency may increase the incidence of star fruit intoxication. Further studies are needed to elucidate the exact mechanisms that cause the neurotoxicity in patients with moderate chronic renal insufficiency.

Brain MRI scans of patients with star fruit intoxication show diffuse or focal lesions of high signal in DWI and low signal in ADC involving the cerebral posterior regions [4,8,9]. The abnormalities are probably caused by cytotoxic edema related to prolonged ictal activity. However, among the five cases reported by Cassinotto et al.[8], only three of them had epileptic seizures. Therefore, whether the MRI abnormalities are directly related to prolonged seizure activity needs further studies to confirm. In our patient, the lesion on follow-up brain MRI after hemodialysis demonstrated a complete resolution of diffusion abnormality. The neuroradiological picture was closely similar to that observed in patients with posterior reversible encephalopathy syndrome RRES, which is not reported from the previously identified cases [4,8,9,10]. The etiology of RPES includes hypertensive encephalopathy, seizures, hypercalcemia, autoimmune disease, medications and toxin [13]. The pathophysiology of PRES is proposed to be vasogenic edema, which may be induced by a breakdown of autoregulation preferentially affecting the posterior circulation [14]. Thus, the unknown neurotoxic substance in star fruit may be responsible for another possible cause of PRES [10].

Early and aggressive hemodialysis has been suggested to be the ideal treatment for star fruit intoxication [2,3]. In severe intoxication cases, continuous methods of replacement therapy may provide a superior initial procedure. Peritoneal dialysis, hemoperfusion and hemofiltration have been considered as effective alternative therapies for star fruit intoxication [3,11,12]. In addition, the presence of seizures in severe cases has been proposed to be associated with a poor prognosis with the mortality rate as high as 75% [4]. Status epilepticus has been reported to subside with extra-corporeal therapies of hemodialysis or hemoperfusion [11,12]. Our patient experienced a good recovery from the neurological symptoms and signs after a session of hemodialysis. Moreover, the abnormal lesion in brain MRI also had a complete resolution after emergency hemodialysis. Therefore, in patients with mild to moderate renal impairment, emergency and aggressive hemodialysis may be a choice for the treatment of star fruit intoxication.

In conclusion, neurological and psychiatric symptoms are common presentations, but are often ignored in star fruit intoxication. Beside uremic patients, star fruit intoxication can occur in patients with mild or moderate chronic renal impairment and may result in a potentially fatal outcome. We thus strongly emphasize that clinicians should be aware that star fruit intoxication must be considered when patients with chronic renal disease, even mild or moderate chronic renal insufficiency, present with unexplained neurological or psychiatric symptoms. Emergency hemodialysis or other replacement therapies may be required for the management of acute intoxication.

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