CASE REPORT

Star fruit intoxication successfully treated by charcoal haemoperfusion and intensive haemofiltration

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We report on a case of an elderly woman with chronic renal impairment, secondary to diabetic nephropathy, who developed a deep coma and seizure shortly after consumption of star fruit. She was managed in the intensive care unit, and her consciousness level improved dramatically after an 8-hour charcoal haemoperfusion and 30 hours of continuous haemofiltration. There were no long-term neurological or renal sequelae 9 months later. Early recognition of this condition, intensive dialytic therapy and supportive measures, as well as early initiation of charcoal haemoperfusion may improve the management of this potentially treatable condition.

Case report

A 76-year-old woman known to have chronic renal impairment secondary to diabetic nephropathy (serum creatinine level of 290 μmol/L, glomerular filtration rate of 15 mL/min/1.73m^2 by Modification of Diet in Renal Disease [MDRD] equation), and diabetic retinopathy was admitted for seizures and drowsiness in May 2007. She had a history of a lacunar stroke in 2002, with a small right internal capsular infarct demonstrated on a computed tomographic scan of her brain. She recovered completely from this with no residual neurological dysfunction. She had been followed up regularly in a general clinic for her medical conditions. On the day of admission, she was found by relatives to be in a state of mental drowsiness at midday. There was a 10-minute period of generalised tonic-clonic convulsion before her arrival at the emergency room, which was self-aborted. She was semicomatose as measured by a Glasgow Coma Scale (GCS) of $E_4V_1M_5$ on arrival at the emergency room. Her blood pressure was high (207/140 mm Hg) and she was tachycardic, with a heart rate of 125 beats/min on the electrocardiogram. She was afebrile. A physical examination revealed no neck stiffness, demonstrated spontaneous movement of all limbs, normal tendon reflexes, and bilateral withdrawal plantar reflexes. Her chest was clear. Her conscious state deteriorated to $E_1V_1M_2$ on GCS 8 hours after admission. The working diagnosis made at that time was recurrent stroke involving the brainstem with an associated epileptic fit. She was admitted to the Acute Stroke Unit for further management. On admission to the Unit, she was in deep coma with no abnormal eye movements and no focal neurological signs suggestive of a brainstem lesion. The differential diagnosis was then revised to either metabolic encephalopathy or meningoencephalitis. Computed tomography of her brain showed an old right internal capsular infarct but was otherwise normal. The white cell count was 11.4 x 10^9 /L, haemoglobin 105 g/L, and platelet count 372 x 10^9 /L. Her blood urea and creatinine levels were 14.1 mmol/L and 319 μmol/L, respectively. There were no major electrolyte disturbances. She was put on intravenous phenytoin for control of her seizures. An empirical meningitic dose of ceftriaxone was started to cover for any central nervous system infection; a lumbar puncture performed later showed no evidence of central nervous system infection. Magnetic resonance imaging of her brain showed no radiological evidence of a brainstem lesion or meningoencephalitis. Her son was interviewed again, and he recalled that she had a similar episode of confusion, which subsided spontaneously, after ingesting star fruit about 10 days previously. He was certain that the patient had eaten two star fruits on the day of admission and was found to be mute with purposeless limb movements about 4 hours after consuming the star fruits. He did not know whether the patient had hiccups before deteriorating. On the basis of this history she was diagnosed with star fruit poisoning with severe neurotoxicity.

The patient was intubated for airway protection, then put on mechanical ventilation and transferred to the intensive care unit for further management. In view of the marked signs of neurotoxicity suggesting a poor prognosis (altered consciousness and seizure), an 8-hour session of charcoal haemoperfusion was commenced, followed by 30 hours of continuous haemofiltration. She had profound hypotension shortly after the initiation of the charcoal haemoperfusion requiring inotropic support in the initial 24 hours. She

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活性碳血液灌流及積極血液過濾治療醫治楊桃中毒

本文報告一名長期患有慢性腎衰竭併發糖尿腎病的年長女性，她進食楊桃後不久陷入深昏迷及出現抽搐。病人被送入深切治療部，經過8小時活性碳血液灌流及30小時連續血液過濾治療後，意識水平大大改善。9個月後並未出現與神經和腎有關的長期後遺症。及早確診、積極透析治療和支援措施，以及盡早施行活性碳血液灌流，都可以提高這種可治癒疾病的診療水平。

developed mild thrombocytopenia (90 x 10^9 /L) without clinical bleeding after the 8-hour charcoal haemoperfusion session. Her GCS started to improve gradually after the charcoal haemoperfusion. There was no recurrence of her neurological symptoms upon cessation of the haemofiltration, and the patient was extubated successfully shortly after the haemofiltration. Upon discharge, she required no anticonvulsants and remained dialysis-independent (recent serum creatinine of 349 μmol/L, glomerular filtration rate of 11 mL/min/1.73m^2 by MDRD method) 9 months after the intoxication.

Discussion

Star fruit belongs to the Oxalidaceae family, species *Averrhoa carambola*. Although available in Hong Kong, star fruit is not particularly popular in the territory. This fruit is common and popular in tropical countries and regions such as Taiwan, India, Thailand, and Brazil. It is widely available in different forms in these countries and regions, such as fresh fruits, in salads, and pickled juice. It consists of sweet and sour types. Star fruit is also used in traditional Chinese medicine as a cough suppressant and diuretic.

Star fruit poisoning was first described in 1980 by Muir and Lam[1] in Malaysia where it was found to have a depressive effect on the central nervous system. Neto et al[2] in 1998 reported six cases of star fruit poisoning in Brazil, with one death after convulsions. They later collected some more cases from other hospitals in Brazil and reported a case series of 32 patients with this form of poisoning.[3] A large majority of these patients had chronic renal failure in the pre-dialysis stage or were on dialysis (either peritoneal dialysis or haemodialysis). This condition is uncommon in those with normal renal function. Only two cases of oliguric acute renal failure have been reported in the literature. These were patients with normal renal function who developed oliguric acute renal failure after the ingestion of large amounts of star fruit juice, either in a dehydrated state or with an empty stomach. Renal biopsies of these two patients showed typical features of acute oxalate nephropathy.[4] The presenting symptoms for star fruit intoxication include hiccups (the commonest symptom, especially in mild intoxication), vomiting, paraesthesiae in the extremities, weakness, insomnia, altered consciousness (confusion or psychomotor agitation), convulsions as well as hypotension, resulting in mortality. Reported mortality rates range from 21% to 40%,[3,5] and mortality is high among those with marked neurological features such as seizures, impaired consciousness, and hypotension. The mortality rate remained high in this subgroup even with supportive measures and intensive dialytic therapy. Possible explanations for these poor outcomes include an initial delay in diagnosing this condition due to the non-specific presentation, the rapid progression of neurological symptoms in some of these patients, and refractoriness to aggressive dialytic treatment. Survivors had no long-term neurological consequences.

There is no consensus at the moment about the ingredient responsible for star fruit's neurotoxicity. Neto et al[3] have shown that intracerebroventricular injection of star fruit extract in rats can induce immediate and persistent tonic-clonic convulsions. Fang et al[6] performed animal experiments and confirmed that the high oxalate contents in star fruit lead to acute oxalate nephropathy in rats. Chen et al[7] first illustrated the dose-dependent neurotoxic effect of star fruit using intraperitoneal administration of saline diluted with star fruit juice. Its neurotoxic effect was markedly reduced when oxalate was eliminated from the star fruit juice before intraperitoneal injection. Fang et al[8] recently demonstrated the important role of oxalate in star fruit neurotoxicity by inducing myoclonus and/or tonic-clonic convulsions in five-sixths of nephrectomised rats fed with either star fruit or oxalate. In humans, however, the possible neurotoxic constituent in star fruit remains obscure. Most investigators propose that there is a powerful neurotoxin in star fruit, which is excreted largely by the kidneys. This neurotoxin is a lipophilic nonpeptide molecule, labelled the neurotoxin fraction (AcTx), and weighs less than 500 daltons.[9] It is lipophilic in nature and can therefore accumulate in blood and cross the blood brain barrier, interfering with the gamma-aminobutyric acid (GABA)-ergic system and inducing neurological symptoms. The chemical nature of this neurotoxin remains largely unknown, but is believed to have a moderate volume of distribution and is not firmly bound to tissue. This neurotoxin can be redistributed in the different body compartments after dialytic therapy, causing recurrence of symptoms shortly after cessation of dialysis especially in intermittent therapy (as short as 2 hours post-intermittent haemodialysis as reported by Neto et al[3]).

These fundamental properties may explain the superiority of charcoal haemoperfusion over other

TABLE 1. Patient outcomes in severe star fruit intoxication treated with different dialysis modalities[3,5,10]

Study	Country/ region	No. of patients with seizure/ impaired consciousness	Treatment modality (No. of patients)*	Outcome
Chang et al,[5] 2000	Taiwan	10 (All with impaired consciousness)	Intensified HD (10)	8 Deaths, 2 survivors
Hospital Authority data (unpublished, 2001)	Hong Kong	1 (Impaired consciousness)	CAPD	Death
Neto et al,[3] 2003	Brazil	7 (All with seizures)	Symptomatic (2)	Death
			CAPD (1)	Death
			CAPD + 2-hour HD (1)	Death
			IPD (1)	Death
			IPD + CAVHD (1)	Death in 10 days
			Conventional HD + CVVHD (15 hours) + daily HD (1)	Survived, recovered after 8 days
Tse et al,[10] 2003	Hong Kong	1 (Impaired consciousness)	Daily HD	Survived

* HD denotes haemodialysis, CAPD continuous ambulatory peritoneal dialysis, IPD intermittent peritoneal dialysis, CAVHD continuous arterio-venous haemodialysis, and CVVHD continuous veno-venous haemodialysis

TABLE 2. Patients with severe star fruit intoxication who were successfully treated with charcoal haemoperfusion[11,12]

Study	Region	No. of patients	Neurological symptoms	Dialysis modality before charcoal haemoperfusion	Time post-charcoal haemoperfusion for recovery in consciousness
Chen et al,[11] 2005	Taiwan	1	Hearing impairment, urinary retention, disturbed consciousness and then coma	Haemodialysis (2 sessions)	Within 1 day
Wu et al,[12] 2007	Taiwan	2	Hiccups, disturbed consciousness then coma; status epilepticus in 1 patient	Haemodialysis (2 sessions)	16-20 hours

forms of dialytic therapy in the management of this form of poisoning.

Choice of dialytic therapy

For mild star fruit poisoning, where there are no neurological symptoms on presentation, intensification of dialytic therapy, by either peritoneal dialysis or intermittent haemodialysis may lead to resolution of symptoms, as well as improved patient survival.[3,5,10] On the other hand, for those with severe neurological symptoms such as impaired consciousness, seizures and hypotension, mortality rates remain high even with the use of aggressive dialytic therapy. Table 1 summarises the outcomes in this subgroup of patients using different dialytic modalities in the four largest series in the literature.[3,5,10] Peritoneal dialysis seems to have consistently inferior treatment efficacy when compared with intensive intermittent haemodialysis. This observation is best illustrated in the series reported by Neto et al.[3]

The role of charcoal haemoperfusion

According to the literature only three patients with severe star fruit intoxication have been successfully treated with charcoal haemoperfusion (Table 2[11,12]). All three patients deteriorated rapidly shortly after ingesting star fruit and had severe neurological symptoms (including impaired consciousness, coma, and status epilepticus) requiring admission to intensive care units for ventilatory support. Their neurological symptoms persisted after conventional haemodialysis but all three patients responded dramatically after 8-hour sessions of charcoal haemoperfusion. They returned to full consciousness within 24 hours of the charcoal haemoperfusion, and they had no recurrence of their neurological symptoms or long-term neurological consequences. These cases have three major implications—the importance of early recognition and risk stratification according to presenting symptoms; the early institution of supportive care, including intubation, mechanical ventilation, and inotropic support; and consideration of using charcoal haemoperfusion to manage patients who are not responding to intensive dialytic therapy. The benefits or otherwise of using charcoal haemoperfusion as a first-line treatment in people with severe neurological symptoms (such as deep coma and seizure) need to be examined with further large-scale studies.

It is difficult to be certain, in our case, whether it was the charcoal haemoperfusion or the haemofiltration that contributed most to our successful management. Our patient started to show an improvement in her GCS shortly after the 8-hour charcoal haemoperfusion ($E_2V_TM_4$ after 2 hours of haemofiltration), and continued to improve upon

completion of the 30-hour haemofiltration session, and had no recurrence of her neurological symptoms upon cessation of dialytic therapy. From the literature review summarised in Table 2, the effects of charcoal haemoperfusion are not evident immediately. All three patients recovered fully within 24 hours of the charcoal haemoperfusion.

There is limited information about the role of continuous dialytic therapy in the literature, but it is probably of low efficacy and requires prolonged treatment. In Neto et al's series,[3] only three patients were given continuous therapy. One patient received continuous arterio-venous haemodialysis (CAVHD) after intermittent peritoneal dialysis and died after 10 days (Table 1); one received conventional haemodialysis, followed by a 15-hour session of continuous veno-venous haemodialysis, and then daily conventional haemodialysis and survived after 8 days (Table 1); one patient presented with mental confusion and hypotension received a 36-hour session of CAVHD, followed by daily conventional haemodialysis and survived after 12 days of dialytic treatment. This suggests that charcoal haemoperfusion is a better management choice than the different modalities of continuous dialytic therapy.

In conclusion, star fruit intoxication should be suspected in patients with chronic renal disease who present with neurological symptoms, especially hiccups, unexplained changes in consciousness, or seizures. This condition is easily missed and may be potentially fatal. The rarity of this condition in our territory may be the result of patient education, but it may also be due to lack of awareness of this condition and/or under-reporting. Risk stratification according to neurological symptoms of patients is essential. Intensification of dialytic therapy, either in the form of peritoneal dialysis or intermittent haemodialysis, should be used to treat mild intoxication. For severe intoxication with impaired consciousness and/or seizures, the early institution of supportive therapy in an intensive care setting, as well as early initiation of charcoal haemoperfusion may improve the management of this potentially treatable condition. Patients with chronic kidney disease should be advised to never eat star fruit and its products.

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