An exotic cause of encephalopathy in a patient with chronic kidney disease

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Practical Implications

Consider star fruit neurotoxicity in the differential diagnosis of unexplained encephalopathy in patients with chronic kidney disease.

An 87-year-old right-handed Asian woman with a history of hypertension, diabetes mellitus, and diabetic nephropathy presented with acute onset of confusion and fatigue for half a day. She became drowsy and incoherent. Occasionally she had twitching in her right hand while using a spoon. At baseline, she was alert and took care of her insulin injections without difficulty. There was no change in her medications. She did not have any travel history. As her symptoms persisted, her daughter brought her to the emergency department.

On examination, the patient's blood pressure was elevated at 207/108 mm Hg and improved with antihypertensive medications. The rest of her vital signs and general examination were normal. She was so drowsy that she barely opened her eyes to verbal stimuli. She could only follow simple commands. She localized to pain and had spontaneous movements in all limbs. The rest of her neurologic examination was nonfocal.

The patient's complete blood count showed normal leukocyte and platelet counts and a low hemoglobin level, 9.9 g/dL (reference range: 12–15 g/dL). Renal function test revealed an elevated creatinine level, 232 μ mol/L (reference range: 49–83 μ mol/L). The abnormal hemoglobin and creatinine levels were within her usual range. Electrolytes, glucose, liver function tests, vitamin B₁₂, thyroid-stimulating hormone, and ammonia were within normal limits. Blood culture was negative. Urine toxicity screen was negative for any recreational drug or sedative medication. Urine culture isolated *Proteus mirabilis*, for which she was started on antibiotic therapy. Electrocardiogram and chest and abdominal radiographs did not show any acute change.

As the etiology of the patient's encephalopathy remained unclear, neurologic workup ensued. Her noncontrast head CT did not demonstrate hemorrhage, massive stroke, or any

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structural abnormalities. Her CSF was clear with a normal opening pressure. The CSF leukocyte count, protein concentration, and CSF to plasma glucose ratio were normal, whereas the elevated erythrocyte count was likely related to trauma tap. The CSF bacterial and acid-fast bacilli cultures did not show any growth. PCR detection for herpes simplex virus type 1 DNA, herpes simplex virus type 2 DNA, and varicella-zoster virus DNA was negative. No malignant cell was found in the CSF.

The patient's EEG recorded a diffuse background rhythm of 3–5 Hz with frequent bilateral periodic lateralized epileptiform discharges at 2–3 Hz that were aborted by 1 mg of IV lorazepam. Her clinical presentation, EEG pattern, and improvement of EEG features with IV benzodiazepine lent support to the diagnosis of nonconvulsive status epilepticus (NCSE).^{1,2} Phenytoin was started.

In the setting of NCSE and chronic kidney disease (CKD), the patient's diet history was investigated. Her daughter confirmed that the patient ate a few slices of star fruit daily for 2 days prior to the onset of encephalopathy. With this additional history, the nephrology team that was immediately consulted for star fruit neurotoxicity recommended hemodialysis. With each dialysis session, the patient became more responsive and the epileptiform discharges on her EEG subsided. After the third dialysis session, the patient sat up in bed, talked to her family members, and passed the swallow evaluation. Soon she was stable for discharge to a rehabilitation hospital.

DISCUSSION

Star fruit (*Averrhoa carambola*) is an exotic fruit especially popular among Asians. While the neurotoxins in star fruit have yet to be determined, they seem to specifically inhibit GABAergic transmission in the brain, resulting in seizures in an animal model.³ Whether from eating the fruit or drinking the juice, star fruit neurotoxicity typically manifests as intractable hiccups, vomiting, encephalopathy, seizures, decreased muscle power, limb numbness, or insomnia.^{4,5} Early hemodialysis appears to be an effective treatment that reduces neurologic sequelae and mortality in patients with CKD.^{6,7} To prevent the potentially fatal complications from star fruit neurotoxicity, patients with CKD should abstain from star fruit.

Etiology for encephalopathy is a common source of consultation for neurologists. Common causes include infection, metabolic derangement, stroke, head trauma, NCSE, neoplasm, iatrogenic process, and autoimmune disease. Here a careful investigation with review of diet led to the diagnosis of star fruit neurotoxicity. As our patient has CKD and cannot eliminate neurotoxins efficiently, providing antiepileptic drug therapy for status epilepticus alone was ineffective. Therefore, we also started the patient on hemodialysis, after which she had an unequivocal improvement.

Star fruit neurotoxicity should be on the differential diagnosis of unexplained encephalopathy in patients with CKD and early treatment with hemodialysis is essential for a good recovery.

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