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Ginkgo Seed Poisoning

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ABSTRACT. A 2-year-old girl presented with vomiting and diarrhea 7 hours after eating a large quantity of ginkgo seeds. She exhibited an afebrile convulsion 9 hours after ingestion. The serum concentration of 4-metoxypyridoxine was as high as 360 ng/mL. Although reported cases of ginkgo seed poisoning usually involve children who exhibit repetitive seizures that can be fatal, prompt administration of pyridoxal phosphate (2 mg/kg) may have prevented additional seizures. This is the first English-language case report measuring 4-metoxypyridoxine concentration during ginkgo seed poisoning. Awareness of the potential danger of overconsumption of this traditional food and its prompt treatment with pyridoxal phosphate may hasten recovery. *Pediatrics* 2002;109:325–327. ginkgo, seed, poisoning, 4-methoxypyridoxine, pyridoxal phosphate.

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ABBREVIATIONS. MPN, 4-methoxypyridoxine; GABA, γ-aminobutyric acid.

The ginkgo seed is a food item commonly eaten because of its nutritive value throughout Japan, Korea, and China. The ginkgo seed is also taken as an herbal medicine for its antitussive and expectorant properties. However, the potential toxicity of the ginkgo seed is not as well-known. With the increasing popularity of oriental cuisine and herbal medicines worldwide, we believe physicians should be aware of possible poisoning caused by 4-methoxypyridoxine (MPN) contained in the ginkgo seed and its treatment with pyridoxal phosphate. We present a case of poisoning in a girl caused by overconsumption of ginkgo seeds. This is the first English-language case report measuring MPN concentration during ginkgo seed poisoning.

CASE REPORT

A previously healthy 2-year-old girl presented to our outpatient clinic with a 2-hour history of vomiting, diarrhea, and irritability. She was afebrile. A tentative diagnosis of viral gastroenteritis was made on initial examination.

Shortly thereafter, a symmetrical generalized clonic seizure without cyanosis occurred, which lasted for 5 minutes, and ceased spontaneously. She retained consciousness immediately after the seizure subsided. Her physical examination, including neurologic examination, remained normal. Emergency laboratory tests included normal complete blood count, routine blood chemistry, and urinalysis; however, blood glucose was elevated at 208 mg/dL. A computed tomography scan of her head was normal. The test of her stool for Rotavirus antigen by enzyme immunoassay was negative.

She was admitted to our hospital for closer observation after her unexplained convulsion. One hour after admission, she vomited again. In her vomitus, we found some pieces of chewed ginkgo seeds. In reply to our inquiry, her parents revealed that she had eaten 50 to 60 pieces of roasted ginkgo seeds (Fig 1) 9 hours before presenting to our hospital. At this time, 2 hours after the seizure, we diagnosed probable ginkgo seed poisoning and administered 30 mg (2 mg/kg body weight) of pyridoxal phosphate intravenously, and 4 mg (0.3 mg/kg) of diazepam rectally.

The next morning the patient had a pleasant disposition and had no gastrointestinal symptoms or neurologic signs. All of the laboratory data including blood glucose were normal. After 4 days of observation, she was discharged without any sequelae. An electroencephalogram performed 40 days later showed no abnormal findings.

We attributed the genesis of seizure to an increased serum concentration of MPN, which is the putative toxic agent in the ginkgo seed. As such, we sent her serum for measurement of MPN concentration to a laboratory, which used a high performance liquid chromatography method.[1] The concentration of MPN measured in her serum drawn immediately after the convulsion was 360 ng/mL. This concentration was remarkably higher than the concentration for blood drawn at both 10 and 82 hours after the convulsion, which were below the detectable limit of 15 ng/mL.

DISCUSSION

In East Asia, the leaves and seeds of the ginkgo tree have been used as food and medicine for >2000 years. Ginkgo seed poisoning attributable to overconsumption appeared in an old Japanese scripture, "*Yamato-Honzo*," written in 1709. The first case of ginkgo seed poisoning documented in a medical

Fig 1. Roasted ginkgo seeds.

journal was in 1881.[2] Vomiting, irritability, and tonic or clonic convulsions were described as the cardinal signs, which usually began 1 to 12 hours after ingestion. During a food shortage in Japan (1930–1960), ginkgo seeds served as an important source of food. Many cases of toxicosis were reported in this period.[3] Toddlers and preschoolers accounted for 74% of these cases and the mortality rate reached as high as 27%.

The origin for the poisoning was originally thought to be cyanide contained within the seed. However, in 1985 it was discovered that the compound MPN could account for its toxicity.[4] γ-aminobutyric acid (GABA) is synthesized from glutamate by the enzyme, glutamate decarboxylase. Because MPN is a competitive antagonist of pyridoxal phosphate, which serves as a coenzyme of glutamate decarboxylase, MPN inhibits the formation of GABA. Thus, overconsumption of ginkgo seeds may have the dual effect to decrease GABA, which is a neurologic depressive transmitter, and increase glutamate, which serves as a stimulant to induce convulsions. Therefore, an effective treatment to prevent seizures is the administration of pyridoxal phosphate to competitively inhibit MPN.[5] Studies have demonstrated that convulsions caused by MPN can be prevented or terminated with pyridoxine.[6]

The number of ginkgo seeds that can be eaten safely by children or adults in a single meal has not been defined. The number of seeds consumed in reported fatalities ranges from 15 to 574 pieces. The exact threshold of MPN concentration that causes convulsions in humans is also unknown. To our knowledge, serum concentrations of MPN taken soon after the time of convulsion have only been reported in 4 cases[7–9] including this case: the lowest concentration was 90 ng/mL[7] and the highest was 484 ng/mL.[8] The fatal dose varies as a poorly defined interaction between the serum concentration of MPN and the individual's nutritious state, especially as it relates to the amount of pyridoxine storage. In our case, the serum concentration of MPN was as high as 360 ng/mL.

Seizures described in previous cases[7–10] were always repetitive. The repetitive nature of the seizures may be explained by the fact that MPN is excreted repeatedly via enterohepatic circulation. Thus, the serum level of MPN may remain high for several hours, prolonging the risk for seizures. Therefore, immediate administration of pyridoxal phosphate is recommended when ginkgo seed poisoning is suspected. Concomitant treatment with anticonvulsants is also recommended.

One piece of raw ginkgo seed contains about 80 μg of MPN.[11] MPN is heat-stable. Therefore, our patient was thought to have ingested about 5 mg of MPN in 50 to 60 pieces of roasted ginkgo seeds. The amount of pyridoxal phosphate 0.25 times that of MPN competes against MPN.[6] Our patient needed >1.25 mg of pyridoxal phosphate; we administered 30 mg that should have been more than adequate. The 30-mg dose is the same amount used for the treatment for dietary deficiency of vitamin B6. Early administration of pyridoxal phosphate and diazepam may have prevented additional seizures that otherwise might have occurred in our case.

Regarding the leaf component of the ginkgo plant, flavonoid glycosides and ginkgolide B contained in the ginkgo leaf may inhibit platelet aggregation and platelet adherence[12] and some case reports of intracranial hemorrhage have been documented as the adverse effects of the ginkgo leaf.[13,14] The child's parents confirmed no leaf ingestion occurred; only the seeds of the ginkgo were eaten.

Oriental cuisine and medicine are becoming popular worldwide. Therefore, physicians need to be aware of the possibility of poisoning from these foods. Physicians should inquire about the foods eaten when patients present with gastroenteritis with or without seizures, especially when treating diverse populations.

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SIMPLISTIC CONCEPT OF THE "GENE" QUESTIONED

". . . Behind the so-called therapeutic gap between genetic screening and medical benefits lies the complexity of the regulatory dynamics that now puts the very concept of the gene into jeopardy. Indeed, 'irony' may be far too weak a word to capture the incongruities of our current situation. For the basic fact is that, at the very moment in which gene-talk has come to so powerfully dominate our biological discourse, the prowess of new analytic techniques in molecular biology and the sheer weight of the findings they have enabled have brought the concept of the gene to the verge of collapse."

Keller F. *The Century of the Gene*. Cambridge, MA: Harvard University Press; 2000

Submitted by Student

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