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**Case Report**
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# CASE REPORT OF LETHAL TOXIN LURKING IN AN EDIBLE PLANT

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## ABSTRACT

Cyanide is notoriously known to the public for more than a century now as a weapon of mass destruction (Zyklon B gas – hydrogen cyanide used by Nazis), an agent for chemical warfare during World War I (hydrogen cyanide) and very infamous "Suicide Pill" used in the past by military and espionage organizations during World War II (potassium cyanide). During the modern industrial era, cyanide poisoning is commonly associated with the industrial exposure and domestic fires. But there is little awareness about potentially fatal consequences of cyanide poisoning from common food sources. Here, we present the case report of a 79-year-old female with acute cyanide poisoning from improperly prepared cassava leaves. Symptoms from ingested toxin may start a few hours after exposure, which include headache, confusion, ataxia, seizures, palpitations, nausea, vomiting, abdominal pain, flushing, and itching of the skin. Patients may develop hypotension, cardiac arrhythmias, renal failure, hepatic necrosis, rhabdomyolysis, and metabolic acidosis; a multisystem manifestation of hypoxia at the cellular level.

Multiple treatment strategies are available to treat cyanide poisoning, including sodium nitrite, sodium thiosulfate, and hydroxycobalamine. This is one of the scenarios where a thorough history, awareness of agents causing cyanide toxicity and knowledge of clinical manifestations can help avoid delays in prompt decision-making for appropriate treatment, thus reducing morbidity, mortality, and prolonged hospital course.

**Keywords:** *cassava; cyanide poisoning; sodium nitrite; hydroxycobalamine; sodium thiosulfate*

Cyanide toxicity from improperly prepared cassava root or leaf ingestion is a rare occurrence in the United States; hence, clinicians should have a high index of suspicion based on the history and clinical presentation. Although no data are available regarding the incidence of cyanide toxicity from edible plant-based food sources, according to the Toxic Exposure Surveillance System, there were 1,301 cases of cyanide toxicity (excluding rodenticides) between 2013 and 2017.[1] Cassava plant is native to South America but is cultivated in many different parts of the world.[2] Food-related outbreak related to cassava has been reported from Uganda in 2017.[3] In this article, we present a patient with cyanide toxicity from improperly cooked cassava leaves. We discuss the epidemiology, clinical manifestations, initial approach, and treatment of cyanide poisoning from cassava.

## CASE PRESENTATION

A 79-year-old female with no past medical history and not on any medications at home was brought to the emergency department at midnight with altered mental status. She had nausea, vomiting, dizziness, and generalized weakness for few hours prior to admission. She has no significant family history. Her daughter gave her Acai juice (acai is a purplish-red berry native to South and Central America and rich in antioxidants and used mostly as over-the-counter health remedy) and Ibuprofen to help her feel better. She checked on her 15 minutes later and found that she had vomited again and was unresponsive. The emergency medical service was called. The patient's initial Glasgow coma scale at the site was 11 out of 15 (eye-opening ¾, verbal response ⅗, motor response ⅚). On the way to the hospital, the patient had one more episode of vomiting. In the emergency department, her heart rate was 90–100 beats per minute, blood pressure (BP) was 80/47 mm of Hg, respiratory rate was 24–26 per minute, and $O_2$ saturation was 98% on Room air (RA). Upon initial emergency physician's assessment, pupils were equal reacting to light, was tachypneic with a respiratory rate of 24–26 per minute, disoriented and responded to physical stimuli and loud voice; abdominal examination was unremarkable; the skin was warm and dry.

Complete blood analysis showed mild leukocytosis with a white cell count of 12.8 K/mm$^3$ (4–12 K/mm$^3$). Renal panel showed sodium 137 mmol/L, potassium 3.9 mmol/L, chloride 100 mmol/L, bicarbonate 17 mmol/L, glucose 344 mg/dL, Blood urea nitrogen (BUN) 25 mg/dL, creatinine 0.89 mg/dL, and anion gap of 20. Initial lactic acid level was 3.8 mmol/L, which later increased to 7.9 mmol/L (0.5–1.6 mmol/L). Computed tomography (CT) head without contrast did not show any acute intracranial findings.

The initial approach in the emergency department was aimed at treating sepsis because the patient had leukocytosis, mild tachycardia, tachypnea, hypotension, and elevated lactic acid levels. The initial investigation was done to identify the possible source of infection. Urine analysis was negative for any signs of urinary tract infection. CT scan of the chest, abdomen, and pelvis was unremarkable. A urine drug screen was negative. Pan cultures came back negative a few days later.

It was at this stage when the patient's family provided certain vital information that changed the course of the patient's management. The patient's daughter reported that earlier that night the patient had eaten cassava leaves grown in one of the family friend's backyard. She only steamed those leaves before eating it (usual practice is to boil it) and admitted to the family that they were bitter. The patient's presentation correlated with cyanide poisoning, including altered mental status, vomiting, tachycardia, tachypnea, hypotension, and metabolic acidosis. Poison control was contacted, and blood cyanide level was sent for analysis, which usually takes several days to come back and has no value in the initial management of the patient with suspected poisoning. Blood cyanide level came back >2.5 mg/L (0.04 mg/L).

The patient continued to remain hypotensive despite aggressive intravenous (IV) fluid resuscitation. Subsequently, the patient was started on intravenous norepinephrine drip through a central venous catheter for hypotension and admitted to ICU. Poison control recommended continuous cardiac monitoring, IV fluids, repeat lactic acid, electrocardiogram in 3 hours, and seizure precautions. Gastric decontamination seemed unnecessary because the patient had ingested cassava leaves a few hours before presentation to the emergency department and had several episodes of vomiting after that. The patient was able to protect her airway and was not intubated. She was placed on 100% high flow oxygen. The patient was treated with "Cyanide Kit" in the ICU, which includes sodium nitrite 300 mg IV and sodium thiosulfate 50 mL of 25% solution to induce methemoglobinemia. Six hours after the treatment, her methemoglobin level was noted to be 16.5%, which trended down to 1% the next day. The patient's BP level and mental status were improved. The patient was discharged in a stable condition with the full neurological recovery after 3 days of the initial presentation.

## DISCUSSION

Cassava (*Manihot esculenta*) is a plant native to South America but is cultivated in many different parts of the world, including Central Africa, Southeast Asia, and China. Cassava root is a major source of carbohydrates in the South American diet, whereas cassava leaves are consumed in the form of soup in Central Africa and Asia.[2]

Cassava leaves, roots (Figure 1), and peels should not be consumed raw because they contain lotaustralin and linamarin which are cyanogenic glucosides. Linamarase is an enzyme present in the cell walls of cassava, which decompose this cyanogenic glucosides liberating hydrogen cyanide which escapes into the atmosphere once roots and leaves are adequately prepared by "wetting method"(flour mixed with water and left in the open for 5 hours).[4] Cassava leaves are usually boiled in the form of soup to be prepared for consumption.

## EPIDEMIOLOGY

There are no data available regarding the incidence of cyanide toxicity from edible plant-based food sources, the number of all-cause cyanide toxicity cases (excluding rodenticides) reported

*[Royalty free image from www.shutterstock.com – link provided below https://www.shutterstock.com/image-photo/tapioca-plants-cassava-closeup-useful-background-83105608]*

**FIG 1**. Cassava Roots and Leaves.

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by the Toxic Exposure Surveillance System ranging from 200 to 300 cases per year. A large number of these cases are related to domestic fires when cyanide is released with the combustion of wool, rubber, polyurethane, melamine, and plastic, found very commonly in household goods. Other edible foods which may contain cyanide are bamboo, macadamia nuts and seeds of apricot, cherry, plum, and peaches.[1]

An outbreak of 98 cases including two deaths was reported in western Uganda from suspected cyanide poisoning in September 2017. Epidemiologic and laboratory investigation revealed the consumption of cassava flour dish made from wild cultivars of cassava with high cyanogenic content as the cause of the outbreak.[3] One of the commonly used medications to treat hypertensive emergencies, sodium nitroprusside is known to cause cyanide poisoning if exposed to light. However, these cases are increasingly rare with widespread awareness about protecting sodium nitroprusside from light and a standard practice to add sodium thiosulfate to the nitroprusside solution.[5]

## CLINICAL MANIFESTATIONS

Signs and symptoms of cyanide poisoning from cassava ingestion depend upon the cyanide content in the root or leaves, which in turn depends upon the type of cassava (there are two types: less poisonous sweet variety and bitter, toxic type) and the preparation method.

Symptoms from ingested toxin may start a few hours after exposure, which may include headache, confusion, ataxia, seizures, palpitations, nausea, vomiting, abdominal pain, flushing, and itching of the skin. Patients may develop hypotension, cardiac arrhythmias, renal failure, hepatic necrosis, rhabdomyolysis, and metabolic acidosis; a multisystem manifestation of hypoxia at the cellular level.[1,3,5,6]

## INITIAL APPROACH AND TREATMENT

Since these cases are rare, thorough history from the patient and high index of suspicion are imperative to diagnose cyanide toxicity from edible plant-based food sources. As cyanide poisoning could be rapidly fatal, emergency assessment and stabilization of airway, breathing, and circulation are priority. Other common causes such as sepsis, drug overdose, hypoglycemia, stroke, etc. should be ruled out. Blood cyanide levels are not helpful initially since it takes several days to report. Most patients have symptoms with blood cyanide levels >0.5 mg/L; levels >2.5 mg/L, like in our patient, would have the risk of coma and death.[6] If the patient presents early after ingestion, gastric decontamination with activated charcoal should be attempted, although there have been reports of the low binding capacity of activated charcoal for potassium cyanide (KCN) *in vitro*.[4]

A treatment strategy to treat cyanide poisoning is to induce methemoglobinemia (Fe2+ to Fe3+) using sodium nitrite. Methemoglobin competitively inhibits cyanide from binding to cytochrome complex and forms less toxic cyanmethemoglobin. Sodium nitrite is dosed according to the patient's hemoglobin level, with the goal to induce at least 15–20% methemoglobinemia.[7,8] Sodium thiosulfate is used as a sulfur donor, which promotes the enzyme rhodanese, which converts cyanide into thiocyanate, which is then excreted in the urine.[8,9]

Hydroxycobalamine, a vitamin B12 precursor, is a better alternative to the approach, as mentioned above, if available. A cobalt moiety present in Hydroxycobalamine avidly binds to intracellular cyanide to form cyanocobalamin, which is readily excreted in the urine.[10,11] Unlike sodium nitrite, hydroxycobalamine does not affect tissue oxygenation and hence can safely be used in victims of the domestic fire who likely have both carbon monoxide and cyanide toxicity.

## CONCLUSION

We report an unusual case of cyanide toxicity from cassava, which is very difficult and challenging to diagnose. This is one of the scenarios where

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a thorough history, awareness of agents causing cyanide toxicity and knowledge of clinical manifestations can help avoid delays in prompt decision-making for appropriate treatment, thus reducing morbidity, mortality, and prolonged hospital course.

## ETHICS APPROVAL

Our institution does not require ethical approval for reporting individual cases or case series.

## INFORMED CONSENT

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

## CONFLICT OF INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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