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## Selected Topics: Toxicology

### MUCOSAL INJURY FROM CALCIUM OXALATE CRYSTALS RESEMBLING ANAPHYLAXIS AND ANGIOEDEMA

Vincent Ceretto, DO, MS\* and Nicholas Nacca, MD\*†

\*Department of Emergency Medicine, University of Rochester Medical Center, Rochester, New York and †Department of Medical Toxicology, University of Rochester Medical Center, Rochester, New York

Corresponding Address: Vincent Ceretto, DO, MS, Department of Emergency Medicine, University of Rochester Medical Center, Rochester, NY 14642

**Abstract—Background:** There are 215 families of plants that contain insoluble needle-shaped calcium oxalate crystals on the surface of their tissues. Upon mucosal contact, injury can cause extreme pain, soft-tissue swelling, salivation, dysphagia, and even aphonia. This presentation can resemble angioedema or anaphylaxis. **Case Report:** A 55-year-old Asian female presented to the emergency department complaining of oral pain, swelling, and numbness. Her family reported that she began to experience sharp pain of the tongue and lips immediately after eating “elephant root.” Physical examination revealed a patient sitting in an upright position, leaning forward with pooling secretions. She had few lingual petechiae, a subtle diffuse erythema, and mild edema of the lower lip. Due to pain, she was unable to speak and swallow. Her vitals remained within normal limits. The patient was taking lisinopril for hypertension. **Why Should An Emergency Physician Be Aware of This?:** Injury by calcium oxalate crystals is a relatively common occurrence that will present to the emergency department. Although most exposures are benign, patients can develop critical illness, requiring emergent therapies and airway management. Due to the nature of presentation, exposure can easily be misdiagnosed as anaphylaxis or hereditary and drug-induced angioedema. Severe pain and the temporal relationship to plant ingestion distinguish insoluble calcium oxalate crystal exposure from these alternative causes of angioedema. There is minimal evidence-based data evaluating treatment of these injuries.

Standard treatment regimen includes a local anesthetic, corticosteroids, opioids, and antihistaminergic agents. Given the relative low cost, ease of administration, and benign adverse effect profile, sodium bicarbonate rinse may have a role as an adjunct therapy, however, research is needed. © 2018 Elsevier Inc. All rights reserved.

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## INTRODUCTION

There are 215 families of plants that contain insoluble needle-shaped calcium oxalate crystals on the surface of their tissues (1). Upon mucosal contact they cause significant pain, soft-tissue swelling, salivation, dysphagia, and even aphonia (2). Historically, these plants were intentionally administered to slaves as punishment or to prevent a witness from being capable of providing verbal testimony (3). The more common *Dieffenbachia* and *Philodendron* spp. can be found in everyday households because of their large beautiful leaves and sustainability with minimal sunlight. Due to their ubiquitous presence, injuries by calcium oxalate crystals are considered to be one of the most common plant-related toxicities. Between 1996 and 1999, there were nearly 11,000 *Dieffenbachia* exposures reported to U.S. poison centers (4). We

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report a case of a severe oral mucosal injury secondary to ingestion of elephant foot yam, *Amorphophallus paeoniifolius*, one member of the family Araceae.

### CASE REPORT

A 55-year-old Asian female presented to the emergency department with significant oral pain, swelling, and numbness. Her family reported that she began to experience sharp pain of the tongue and lips immediately after eating “elephant root.” The vegetable was given to her family by an acquaintance. The preparer sliced the raw root into pieces and added it to a stir-fry. This person reported tingling of his fingers after he handled the root. He did not eat the root. The patient denied pruritus, hives, abdominal pain, chest pain, and dyspnea. She never had experienced a similar event in the past and had never eaten this root before. Physical examination revealed a patient sitting in an upright position, leaning forward with pooling secretions. Examination of the patient’s oral mucosa revealed few lingual petechiae, a subtle diffuse erythema, and mild edema of the lower lip. Due to pain, she was unable to speak and swallow. Her vital signs were as follows: blood pressure of 135/79 mm Hg; heart rate of 77 beats/min; respiratory rate of 20 breaths/min; temperature of 36.5°C; oxygen saturation of 100% on room air. The patient’s only medical history was hypertension, for which she was taking lisinopril.

The differential of the treatment team included anaphylaxis and angiotensin-converting enzyme inhibitor (ACEI)-induced angioedema. The patient was treated with 0.3 mg intramuscular epinephrine once, 10 mg intramuscular dexamethasone, 50 mg intramuscular diphenhydramine and 20 mg oral famotidine. After consultation with toxicology and identification of the injurious plant, the patient was treated with 5 mL 2% lidocaine solution.

Although the patient’s pain only mildly improved, she was able to open her mouth and her drooling decreased. She was admitted to the hospital for observation. Her symptoms continued to improve and the following day she was able control her secretions, tolerate fluids by mouth, and speak in short sentences. She was discharged within 24 h with prescriptions for 2% lidocaine mouthwash every 8 h as needed for pain and 40 mg prednisone once daily for 5 days. On follow-up, the patient reported severe pain for the first 4 days, during which she maintained a liquid diet. On day 4 post ingestion, when able to open her mouth fully, she noted a white film on her tongue and buccal mucosa (Figure 1). On day 10 post ingestion, she was able to tolerate soft foods but reported new abdominal discomfort that lasted 1 week. At 1 month post ingestion, the patient was asymptomatic.



Figure 1. Oral mucosa 4 days after injury by calcium oxalate crystals of *Amorphophallus paeoniifolius*, elephant foot yam.

### DISCUSSION

Elephant foot yam or *Amorphophallus paeoniifolius*, is a species of plant in the Araceae family. It is considered a staple food in India, Philippines, Indonesia, Sumatra, Malaysia, Bangladesh, China, and other Southeast Asian countries. This plant grows well in aerated coarse-textured soils that receive adequate rainfall (Figure 2) (5). The edible corm or underground plant stem can weigh up to 9 kg and is rich in carbohydrates, protein, vitamin A, calcium, and phosphorus (Figure 3) (5,6). Once cultivated, corms can be stored for several months



Figure 2. *Amorphophallus paeoniifolius*. Photo by Bilal Ahmad, MBBS.



**Figure 3. Elephant foot yam. Photo by Bilal Ahmad, MBBS.**

without spoiling, thus allowing this vegetable to be easily exported (5,6). They are difficult to find in the United States, but can be purchased online or at Asian markets that import the vegetable. Elephant foot yam is well known for its acrid taste and injurious potential when eaten raw. This is because the plant contains needle-shaped calcium oxalate crystals on its surface. To render the plant safe to eat, the vegetable is boiled or baked.

There are five categories of crystals based on shape and morphology and include crystal sand, raphides, druse, styloid, and prismatic (7). Their function is thought to include calcium regulation, electrolyte balance, plant protection, tissue support, detoxification of heavy metals or oxalic acid, and light gathering and reflection (7,8). Raphides or needle-shaped calcium oxalate crystals are well known for their defensive properties against herbivores. Anywhere between 100 and 2000 of these raphides are located within specialized cells called the idioblast (9). Upon contact with cellular barriers (e.g., epithelium, cell membranes), each raphide fires as a single projectile, one at a time, for a distance of two to three cell lengths (10). It is now thought that upon penetration, ejector cells simultaneously release a protein, likely a protease, which synergistically causes tissue damage and swelling (11,12).

Exposure to injurious calcium oxalate crystals is common worldwide, especially in children who curiously place foreign objects in the mouth. Symptoms in general are minimal and self-limited. In one report of nearly 200 Araceae exposures called into a single poison center, only 4 patients developed symptoms and all were mild (13). In another report of nearly 11,000 calcium oxalate exposures identified at poison centers, only 34.7% of the patients developed symptoms. Overall, oral pain and

irritation were the most common symptoms, followed by dermal pain from handling the plant. The same authors reviewed all accessible case reports before 1999 and compared this to the symptoms reported from calcium oxalate exposures within the poison center data. They found that of these case reports, 29.6% developed aphonia, 48.1% developed respiratory obstruction, and 11.18% died, whereas none of these findings were reported in the poison centers (4). The observed discrepancy likely underlines publication bias associated with the severity of illness regarding these exposures. The data in the animal kingdom similarly show significant lethality after exposure. In a case report of 72 cat exposures to *Philodendron* spp., death was reported in 37 cases (14).

There are several features of calcium oxalate injuries that distinguish them from angioedema and anaphylaxis. Symptomatic calcium oxalate injuries present with hyperacute pain, almost immediately or shortly after touching a part of the plant with the oral mucosa and skin. This pain likely results in dysphagia, aphonia, and pooling secretions. This is exemplified in this case report as well as several others (15–17). Patients with allergic, ACEI-induced, or hereditary angioedema may describe a tingling or burning sensation from the swelling, but pain is a much less common complaint (18). In these cases, it is the mucosal swelling that is most prominent and leads to the associated complications, such as airway compromise. Additionally, histamine-induced angioedema and anaphylaxis are associated with hives, abdominal pain, and pruritus, whereas calcium oxalate causes a localized injury in isolation of these other findings. Lastly, calcium oxalate injuries may cause delayed wound healing and oral burns (Figure 1).

Current pharmaceutical recommendations for treatment include local anesthetics, corticosteroids, opioids, and antihistaminergic agents, but there is little evidence to support their efficacy. For example, though diphenhydramine is often one of the primary pharmaceutical interventions, multiple animal studies have shown only minimal or no improvement in reducing soft-tissue swelling after injury (19,20).

In 2011, Dip et al. evaluated treatment efficacy by using multiple medications to treat edema after exposure to the *Dieffenbachia picta*. Sap of the plant was placed on rat tongues and after 15 min, authors administered dexamethasone, promethazine, indomethacin, eugenol, or verapamil by an intraperitoneal injection. According to their results, eugenol was significantly better than all of these medications. The other medicines showed minimal to moderate efficacy, with dexamethasone resulting in the least improvement (2). Intravenous or intraperitoneal eugenol extract was also more efficacious than intraperitoneal dexamethasone, intravenous promethazine, and

intravenous epinephrine combined; a similar regimen used to treat anaphylaxis (21). Eugenol, a xenobiotic found in clove oil, is primarily used in dentistry as an anesthetic and antiseptic agent. Its use is limited due to serious side effects, including hemorrhagic pulmonary edema and seizures (22).

There are many sources that report calcium oxalate crystals can be inactivated, and for those indigenous to this plant, it is common knowledge to have a recipe to prevent and treat injury. If each calcium oxalate crystal is expelled one by one from an idioblast and each contain their own ejector cells and injurious protease, then perhaps inactivating this structure would prevent further tissue injury. In 1940, the *Malayan Agricultural Journal* published an article titled “The Malayan Keladis and Other Edible Aroids.” Per the author’s recommendations “should the acidity be accidentally tasted thick syrup of sour lime or tamarind or solid tamarind with or without salt or even bicarbonate of soda will allay it” (23). The recommendation suggests that washing ones mouth with an acid or a base after exposure can limit toxicity. Research has demonstrated that the raphides are susceptible to breakdown by both heat and acidity. Boiling these injurious plants to 100°F for 5 min prevented injury, as did pretreating the sap with sodium bicarbonate (2,20). Unfortunately, there is no research that evaluates swelling after injury with the use of sodium bicarbonate or another base.

### WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

Injury by calcium oxalate crystals is a relatively common occurrence that will present to the emergency department. Although most exposures are benign, patients can develop critical illness, requiring emergent therapies and airway management. Due to the nature of presentation, exposure can easily be misdiagnosed as anaphylaxis or hereditary and drug-induced angioedema. Severe pain and the temporal relationship to plant ingestion distinguish insoluble calcium oxalate crystal exposure from these alternative causes of angioedema.

There is minimal literature and conflicting data regarding treatment of these injuries. Standard treatment regimen includes a local anesthetic, corticosteroids, opioids, and antihistaminergic agents. Given the relative cost, ease of administration, and benign adverse effect

profile, sodium bicarbonate rinse may have a role as an adjunct therapy; however, research is needed.

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