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Intravenous lipid emulsion may have played a key role in treating Daisy's toxicity emergency.



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CASE REPORT CHALLENGE

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CASE REPORT: TOXICOLOGY

A “Phantom” Toxicosis

**MEET THE AUTHOR**

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Exposure to toxins is not always observed or discovered until after clinical signs appear. This article describes a case of toxicity discovered only after 2 dogs had died and clinical signs appeared shortly thereafter in a third dog in the same family.

THE CASE

A 4-year-old spayed female Labrador retriever, whom we will call Daisy (patient name changed to protect clients' privacy), was brought to the University of Florida emergency service for suspected toxicity. The clients reported that 2 hours earlier, when a family member arrived home from school, all 3 family dogs were acting perfectly normal. She took them for a leash walk and brought them back inside the house. Approximately 1 hour later, the Labrador still appeared to be acting normally, but the 2 housemates (a 1-kg intact female chihuahua and a 9-kg neutered male Jack Russell terrier) began panting, vomited multiple times, and then exhibited a stiff gait in the hind limbs. The vomitus was described as frothy fluid with a red tinge. Within 1 hour of the initial clinical signs, both small breed dogs collapsed and died. After the death of her housemates, the patient began panting and appeared to be distressed. She had no previous medical conditions and was not receiving any medications. The clients were unaware of any exposure to toxins or access to medications or drugs in the house, and did not notice anything disturbed that might indicate that the dogs had gotten into something.



During initial examination at the hospital, Daisy was alert, responsive, and ambulatory. She weighed 27 kg and her rectal temperature was very high, at 108.6°F (reference range [ref.] 99.5°F to 102.5°F). Her heart rate was slightly elevated at 180 beats/minute (ref. for a large breed 60 to 120 beats/minute), and no heart murmur or arrhythmia was auscultated. Femoral pulses were bounding yet synchronous, and mucous membranes were injected. Daisy was panting heavily, but her lung sounds were clear. She was moderately hypertensive; systolic Doppler blood pressure was 170 mm Hg (ref. 90 to 140 mm Hg).

Initial interventions included active external cooling with a cool water bath and fans. Because clinical dehydration had been suspected during physical examination, an 18-gauge IV catheter was placed and 1 L of lactated Ringer solution was administered as a bolus, followed by maintenance at 177 mL/kg/day. Initial diagnostics included complete blood count, blood chemistry, and venous blood gas analysis, all yielding normal results. General anesthesia was induced to control Daisy's airway, aid the cooling effort, and prepare for gastric lavage. The induction agent was propofol (8 mg/kg IV), and inhalation anesthesia was maintained with isoflurane, delivered with oxygen at 1.5 L/minute. For enhanced cooling of the inspired gas, the breathing circuit tubes were passed through ice water. Monitoring during anesthesia consisted of electrocardiography, pulse oximetry, capnography, and blood pressure measurements; all values remained within normal limits.

Sorbitol is a cathartic agent, which can hasten elimination of bound toxins by defecation.



Gastric lavage produced fluid with a small amount of partially digested food. For delivery of activated charcoal with sorbitol (2 g/kg) into her stomach, a nasogastric tube was placed. Activated charcoal can decrease absorption of toxins in the gastrointestinal (GI) tract and reduce toxin exposure that could continue via enterohepatic recirculation.¹ Sorbitol is a cathartic agent, which can hasten elimination of bound toxins by defecation. To facilitate the placement

process, we inserted the nasogastric tube while Daisy was anesthetized and left it in place after recovery so subsequent doses could be administered in case decreased mentation precluded oral administration. We also administered a dose of maropitant (1 mg/kg SC) to decrease the risk of vomiting. To bind any fat-soluble toxins that Daisy may have been exposed to, we initiated intravenous lipid emulsion (ILE) therapy with a bolus of Intralipid (Baxter Healthcare Corp., baxter.com) at 1.5 mL/kg IV.

We discontinued cooling after 15 minutes, when serial rectal temperatures indicated that Daisy's temperature had decreased to 103.4°F. During recovery from anesthesia, she regurgitated a large volume of activated charcoal, necessitating suction of the oropharynx. The endotracheal tube cuff was deflated and the tube was removed. After 10 minutes, Daisy's body temperature normalized and recovery was otherwise uneventful.

Overnight monitoring included frequently taking Daisy's rectal temperature to ensure that she remained normothermic. Vital parameters and blood pressure were monitored every 12 hours and remained within normal limits. To protect against bacterial translocation from the GI tract and to provide coverage based on the possibility of aspiration during the regurgitation event, a broad-spectrum antibiotic (ampicillin/sulbactam, 30 mg/kg IV q8h) was added to the treatment protocol. Pantoprazole (1 mg/kg IV q12h) was given to protect against formation of gastric ulcers. Eight hours after the initial administration of activated charcoal, we administered another dose at 2 g/kg, this time without sorbitol, via the nasogastric tube. ILE therapy was continued via constant rate infusion at 15 mL/kg IV for 1 hour and repeated 6 hours later. During the night, Daisy produced a formed, black bowel movement, which was attributed to the activated charcoal.

The next day, Daisy's vital parameters remained within normal limits and her mentation seemed to be normal. Because she appeared to be euhydrated, we decreased her IV fluid rate to 70 mL/kg/day and offered her food. She ate readily, so we discontinued the IV fluids and transitioned her from IV ampicillin/sulbactam to oral amoxicillin trihydrate/clavulanate potassium (500 mg q12h). Normal urination was observed during her walks outside.

On the second day of hospitalization, Daisy's vital parameters and appetite continued to be normal. A recheck of her complete blood count revealed mild



eosinophilia (1.42 K/ μ L, ref. 0.1 to 1.3K/ μ L), possibly attributable to inflammation. Moderate lipemia and hemolysis were also noted, possibly a result of the ILE infusions. A recheck of blood chemistry showed mild elevation of liver enzymes (ALT [alanine transaminase] 180 U/L, ref. 18 to 64 U/L; AST [aspartate transaminase] 211U/L, ref. 15 to 52 U/L) but was otherwise unremarkable.

Given the response to early decontamination and supportive care, Daisy was discharged 36 hours after presentation and fully recovered from the event. Because the gastric fluid produced during stomach lavage was too dilute for analysis, we submitted gastric contents from her deceased housemates to an outside laboratory for gas chromatography mass spectrometry analysis. The result was positive for chlorfenapyr, a pesticide that is classified as moderately hazardous by the World Health Organization.²

DISCUSSION

The source of Daisy's chlorfenapyr exposure was never determined. According to the clients, they did not have chlorfenapyr in their house or yard, nor had their home or yard received pest control services. None of the 3 dogs were seen eating grass, and there was no grass in the vomitus from the 2 housemates or in the gastric lavage fluid from Daisy. The poisoning could have resulted from application by a nearby resident unaware of the hazard that it would pose or by someone with malicious intent.

Since the cause of Daisy's acute onset of clinical signs was unknown and because the 2 other dogs in the house died suddenly, we performed decontamination along with active cooling techniques early to address her hyperthermia and suspected intoxication. Hyperthermia can lead to many complications, including compromise of the GI mucosa, bacterial translocation, sepsis, and central nervous system damage.³ Severe hepatocellular damage can lead to decreased production of clotting factors and increased risk for hemorrhage. The patient was also at risk for development of systemic inflammatory response syndrome, which can lead to disseminated intravascular coagulation (DIC). Clinical signs of thrombocytopenia resulting from DIC include petechia, ecchymosis, and hematochezia. Ischemic injury to myocardial cells can lead to cardiac dysfunction and arrhythmias. Damage to pulmonary endothelium could cause noncardiogenic pulmonary edema and respiratory dysfunction. Renal injury can

occur if significant muscle damage develops and rhabdomyolysis ensues. In small animals, common toxins that can induce severe hyperthermia if ingested include strychnine and metaldehyde.⁴ However, in this case, no muscle rigidity (as occurs with strychnine) and no convulsions (as occur with metaldehyde) were seen. Heatstroke was initially on the differential diagnosis list, but Daisy had been resting normally for approximately 2 hours before symptoms suddenly developed. Because of Daisy's severely elevated body temperature, along with the acute death of the 2 other dogs, the initial prognosis was guarded, for concern that multiple organ dysfunction syndrome might develop.

Use of ILE is indicated when exposure to a lipid-soluble toxin is suspected. Although the exact mechanism of action for ILE has yet to be determined, the predominant theory involves the concept of a lipid sink. Infused ILE creates an intravascular lipid phase in the blood, which acts as a sink for lipophilic drugs and pulls the toxic substances out of the tissues, thereby enhancing their elimination. It has been speculated that ILE may also move fatty acids into the mitochondria to provide adenosine triphosphate (ATP), which counteracts the risk for cell death.⁵ Potential adverse effects of ILE therapy include sepsis secondary to bacterial contamination, thrombophlebitis, hyperlipidemia, hemolysis, and pancreatitis.

CHLORFENAPYR TOXICITY

Chlorfenapyr is a lipophilic miticide insecticide, categorized in a unique class of chemicals called pyrroles. It works by removing the N-ethoxymethyl group through microsomal oxidation, thereby altering ATP production.⁶ This action releases the corresponding free pyrrole, which is a lipophilic weak acid. The uncoupling of oxidative phosphorylation in the mitochondria causes energy to be released as heat instead of stored as ATP.⁷ This process explains the hyperthermia that was observed in this patient. Left unchecked, this process will ultimately lead to cell dysfunction and subsequent cell death.

Numerous cases of chlorfenapyr poisoning in humans, with several fatalities, have been reported.⁸⁻¹⁰ However, to our knowledge, no reports of confirmed chlorfenapyr toxicity in a veterinary patient have been published. We suspect that all 3 dogs reported here were exposed, because although the chlorfenapyr was confirmed in a housemate's stomach, not the patient's, the clinical signs for all 3 dogs were similar.

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Hyperthermia and tachypnea are also prevalent among humans who have ingested chlorfenapyr. In those cases, treatment consisted of gastric lavage and activated charcoal administration only.

In our case, the use of ILE therapy probably contributed to Daisy's successful outcome because chlorfenapyr is lipophilic. A veterinary report of using ILE therapy in a dog to treat bromethalin toxicity, which has a similar mechanism of action to that of chlorfenapyr, has been recently published.¹¹

In 2001, the U.S. Environmental Protection Agency approved the use of chlorfenapyr on nonfood ornamental plants grown in greenhouses.⁶ However, chlorfenapyr can also be purchased by consumers online or in some stores. It is marketed under various product names, including Phantom and Pylon. For this reason, the veterinary community needs to be aware of this dangerous compound. **TVN**

This case has been previously published by the veterinarians who managed it: Davies RB, Campos S, Lynch AM. Acute chlorfenapyr toxicity in 3 dogs from a single household. J Vet Emerg Crit Care (San Antonio) 2019;29(6):686-689.

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