Pacific Tide

An informational newsletter

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February 2015
Volume 2, Issue 1

About our Author

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Dr. Kurek graduated from UC Davis School of Veterinary Medicine in 2009. She completed a rotating small animal internship at the University of Pennsylvania in 2010, where a dynamic emergency caseload provided her with a wide breadth of experience in emergency medicine, trauma, and critical care. Her special interests include emergency surgery, trauma, infectious disease, and wildlife medicine. She joined PVSES in August 2010. She is excited to be helping animals back near her hometown and spends her life outside of work with her husband Kyle, two gorgeous children, two spoiled labradors Sandy and Ebony, and their kitties. She also enjoys backpacking, dance, running, and water sports in her free time.

Jessica Kurek, DVM

Cholecalciferol Rodenticides: A Case Study

By: Jessica Kurek, DVM

Rodenticide toxicity occurs far too commonly in our pets, especially dogs. In recent years the majority of toxicities have been anticoagulant rodenticides treated with decontamination, Vitamin K supplementation, and blood product transfusions as needed. These toxicities are expensive to treat if patients are already bleeding, and can cause acute fatalities if bleeding occurs into certain locations (brain, lungs, etc.). As many vets are aware, a new California ban on sale of certain anticoagulant rodenticides went into effect last July. Our pets will still be at risk from anticoagulant type rodenticides due to use by pest control companies and baits purchased prior to the ban. However, we are likely to see a notable shift in the types of rodenticide toxicities we treat in the coming years. Therefore it is important to be aware of WHICH type of rodenticide a patient was exposed to and to treat them accordingly.

Meet Mikey: a 6 1/2 year old male neutered Labrador who presented to the Pacific Veterinary Emergency Service for evaluation of acute onset of vomiting, tenesmus, soft stool, and lethargy, with a possible days-weeks history of polyuria, polydipsia, and mild lethargy. Physical exam revealed mild tachycardia, heavy panting, an uncomfortable abdomen, an episode of regurgitation during exam, and liquid stool on rectal. Initial diagnostics showed a severe hypercalcemia with total calcium of 15.6 and ionized calcium of 1.75 with mild azotemia (BUN 26, Crea 2.5). His phosphorus was normal. Vit D type rodenticide was known to be placed on the property by a gardener, but the owners initially thought Mikey did not have access to the bait. Exposure to human medications containing significant amounts of Vitamin D was unlikely; Vitamin D containing sunscreen was used by owners but ingestion of large amounts was not possible. The reported longer term history of lethargy and unknown duration of PU/PD created concern for other underlying causes of hypercalcemia.

The most common source of cholecalciferol (Vit D3) toxicity is rodenticide ingestion, however oral vitamin D supplements and topical skin products can cause a similar clinical syndrome. Once ingested, cholecalciferol is metabolized by the liver and then kidneys to the most active metabolite 1,25-dihydroxycholecalciferol (calcitriol). Calcitriol increases calcium levels in several ways, including absorption of calcium from the GI tract, increased bone resorption of calcium, and increased calcium absorption in the renal tubules. Increased serum calcium and phosphorus levels can lead to mineralization of multiple soft tissues, most notably renal, cardiovascular, and gastrointestinal systems. Clinical signs of cholecalciferol ingestion generally occur within 12-36 hours and include vomiting, weakness, lethargy, melena, hemorrhagic diarrhea, depression, PU/PD and death. Differentials include hypercalcemia of malignancy (lymphoma, anal sac adenocarcinoma, others), primary hyperparathyroidism, hypoadrenocorticism, chronic renal failure, other acute renal toxins (grapes/raisins, ethylene glycol, etc.), and granulomatous disease.

Mikey's initial therapy consisted of diuresis with twice maintenance 0.9% sodium chloride IV, gastrointestinal protectants, Lasix, and prednisone. Ultrasound of the neck and abdomen showed mildly hypoechoic nodules in the cranial poles of the thyroid glands bilaterally and an enlarged spleen. Splenic aspirate revealed extramedullary hematopoiesis with mild reactive lymphoid hyperplasia. Chest radiographs were normal. Additional bloodwork was submitted to Michigan State University to assess ionized calcium, Vitamin D, Parathyroid (PTH), and PTH related peptide (PTHrp) levels. Mikey was treated with pamidronate (2 mg/kg IV) the day after presentation, when his ionized calcium had increased to 1.96. Fluid rate was increased to 3.5x maintenance and prednisone and Lasix doses were increased further. His ionized calcium level was higher the following morning (2.21), then improved gradually over the first weekend with periodic spikes. The owner determined that their gardener had been carrying an open bucket of cholecalciferol bait around the yard while filling bait boxes on the day that Mikey's signs started. Michigan State testing results confirmed cholecalciferol toxicity with extremely elevated Vit D levels (2040 nmol/L after dilution with normal 60-215 nmol/L), negative PTHrP levels

and a PTH level of 0. After consulting with the rodenticide manufacturer, fluid rates were increased further to 5 times maintenance, prednisone was increased to >2 mg/kg BID and furosemide was increased to 4 mg/kg TID. Pamidronate was repeated 4 more times during Mikey's stay, at 3-5 day intervals. Cholestyramine was recommended by poison control and used for 3 days at 0.3 gm/kg PO q8. Mikey disliked the cholestyramine and appetite was decreased, so it was not continued beyond 3 days.

If cholecalciferol ingestion cannot be initially confirmed (as with Mikey), then additional diagnostics should be pursued to rule out neoplasia (abdominal ultrasound, CBC with clin path review, chest rads, PTHrP levels, etc), primary hyperparathyroidism (thyroid ultrasound, PTH and iCa levels), and other potential causes of hypercalcemia. Even with known cholecalciferol ingestion, Vit D testing should be submitted to help give owners an estimate of severity of ingestion and required duration of therapy.

General treatment recommendations for cholecalciferol toxicity include:

- Decontamination:
  - Emesis or gastric lavage (if recent ingestion)
  - Activated charcoal q8 hours for 1-2 days to interrupt enterohepatic circulation (first dose with a cathartic). Repeat usage of AC in this manner has become controversial and some poison control toxicologists recommend only 2 doses to avoid electrolyte disturbances.
- Promote calciuresis with
  - Aggressive fluid therapy with 0.9% NaCl at 2-3 times daily
    - Rates up to 5x maintenance may be indicated for effective calciuresis
  - Furosemide at 2-4 mg/kg PO q8 or a CRI
  - Prednisone 2-3 mg/kg PO q12 or dexamethasone 0.2 mg/kg IV q12
- Phosphate binders (Aluminum hydroxide) if hyperphosphatemia is present and Ca x P product is greater than 60-70.
- Bisphosphonates to decrease bone resorption of calcium
  - Pamidronate most commonly used. Dose = 1.3 - 2 mg/kg IV diluted in saline and administered over 2 hours.
    - Takes 24-48 hours for Ca and P levels to decrease
    - Can repeat q5-7 days or q3-4 days in cases of very large ingestion
    - Treatment may be required for <u>weeks</u> due to high lipid solubility and a long terminal half life (weeks to months).
- Anti-emetics and GI protectants prn to prevent vomiting and maintain good appetite
- Low calcium diet
- Monitoring of calcium levels (both ionized and total), phosphorus, and renal values q24-48 hours during hospitalization

Several other treatment options are reported:

- Cholestyramine
  - Bile acid sequestrant routinely recommended by poison control if recent exposure
  - Was recommended for Mikey 1 week post-exposure
  - Dose = 0.3-0.5 grams/kg q8 hours x 3-5 days
  - Provided as a sugary orange flavored powder that must be dissolved in liquid. Anecdotally has poor palatability for dogs leading to significant GI upset
- Salmon calcitonin
  - Used in addition to bisphosphonates as standard of care in human cases of hypercalcemia
  - Limited data shows a poor outcome in veterinary patients when these two drugs are used together
  - Most resources do not recommend the use of calcitonin unless pamidronate is ineffective

(Continued on page 4)

Intralipids

Since cholecalciferol is fat soluble, lipid therapy may have theoretical use

No available data or consensus on when/if lipids should be used for this toxicity.

Mikey's calcium levels reached a normal level (total and ionized) after 5 days of hospitalization (4 days following first pamidronate dose). Hypercalcemia was present again by the following day and continued to vary with borderline azotemia for the next week. After 2 weeks in the hospital, we began a slow weaning of fluids, Lasix, and prednisone. Pamidronate was repeated several times, as described earlier, and decreases in iCa levels were noted 24-48 hours after subsequent doses with recurrent elevation after first three doses. After 18 days of hospitalization Mikey was finally discharged with a normal calcium level (off of fluids and lasix) and upper normal renal values. Continued treatment included prednisone at 0.25 mg/kg/day, omeprazole, prazosin, baytril (for UTI) and metronidazole (for diarrhea). Mikey experienced multiple medical complications during his treatment, which should be considered when treating a patient with high dose cholecalciferol toxicity. These problems included:

Excessive polyuria requiring walks q30-60 minutes, close weight monitoring, and ultimately urinary catheter placement due to signs of detrusor atony/overflow.

High IV fluid rates were not tolerated by peripheral catheters, leading to peripheral edema, perivascular irritation, and bruising. A jugular catheter was placed for long term therapy and was well tolerated. Perivascular bruising and edema occurred at site of second pamidronate dose, likely due to extravasation of drug.

Prednisone side effects at the administered doses were significant. Most problematic for Mikey (in addition to polyuria sequelae listed above) were mild transient hyperglycemia and severe anxiety, restlessness, and panting that were only partially managed with anxiolytics and sedatives (alprazolam). Ultimately these effects required early dose reduction of prednisone.

Urinary tract infection. Mikey had a history of UTIs, but urine dilution from diuresis, urinary retention, and urinary catheter placement all put him at risk for the UTI he developed during treatment.

Hypertension - required amlodipine therapy temporarily, likely due to high fluid rates

Variable appetite, intermittent diarrhea, occasional vomiting - managed with medications, as needed

Mikey was initially rechecked every 2-3 days after discharge. His recheck ionized and total calcium levels were initially mildly elevated, but are now normal at 1.5 months post-ingestion. Vit D level was still elevated 25 days following admit to the hospital at 755 nmol/L. Azotemia and UTI resolved. We will continue to wean his prednisone dose and recheck his labwork weekly until normal calcium is maintained without steroid therapy. Long term impaired renal function may be present, although we are hopeful that soft tissue mineralization was minimal since hyperphosphatemia was never documented. Renal values and urine specific gravity should be monitored in the future.

There are several important things to learn from Mikey's case. First, the treatment for high dose cholecalciferol toxicity can be very intensive and ideally requires 24 hour care due to high levels of diuresis (Mikey went through 10-12 LITERS of fluids daily), management of polyuria, frequent dosing of medications, and potential for treatment complications. Second, this treatment can be very costly for owners, both emotionally and financially. Long term prognosis is guarded in cases where soft tissue mineralization has occurred, as this can lead to significant organ dysfunction. Finally, as with all of our rodenticides, client communication to prevent use of these toxins within reach of pets is very important. As the types of rodenticides used shift to cholecalciferol and neurotoxins such as bromethalin, strychnine, and zinc phosphide, we will unfortunately be seeing more of these potentially complex cases.

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About Our Hospitals

Pacific Veterinary Specialists was founded to provide high quality, specialized medical care to companion animal patients. Our practice is dedicated to serving the veterinary community as a partner in total patient care. We offer comprehensive specialized services including video endoscopy, Doppler ultrasound, surgery, 24-hour ICU care, and emergency and critical care. Our staff is committed to providing compassionate and thorough medical care that meets the needs of the patient, client, and referring veterinarian. In September 2011 we opened PVSM and currently offer internal medicine appointments and same day referrals, Tuesday through Thursday in Monterey. Behavior consultations by appointment are available on Mondays.

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