Uncommon but potentially devastating

By Amy Weeden

Two recent cases of vitamin D toxicity presented to Gribbles Veterinary prompted a further investigation of this seldom-seen problem.

Case one – the baited cat
A year-old, adult spayed female cat presented with a three-day history of anorexia and lethargy. She was an avid hunter of rabbits, rats and mice.

The clinical exam was unremarkable. Pertinent findings from a laboratory investigation included a markedly increased total calcium of 4.47mmol/L (2.00–2.95), mild azotaemia (a mild increase in blood urea nitrogen, and creatinine at the upper end of the reference interval) and mildly increased red cell mass, suggesting dehydration.

The cat was discharged after supportive care, with a plan for her to return for repeat blood work to confirm the marked hypercalcaemia. The revisit showed essentially no improvement and no change in the calcium level. After further questioning the owner did some investigating and found that Feracol possum bait stations had been placed in the neighbourhood.

The cat was then hospitalised, and treatment for presumptive cholecalciferol toxicity was initiated with activated charcoal, intravenous fluids, furosemide and prednisone. The azotaemia resolved over a couple of days but the hypercalcaemia reduced very slowly. A bisphosphonate drug was added for its calcium-lowering effect.

After a week of hospitalisation the cat's calcium levels returned to normal. She was discharged on subcutaneous fluids and tapering doses of prednisone and furosemide for the following week and a half. The hypercalcaemia resolved completely. There was a persistent mild increase in blood urea nitrogen, suspected to be due to the cat's high-protein diet, as she remained a frequent hunter.

Case two – the beached dog
A couple of months later, a seven-year-old neutered dog presented to the same veterinarian with vomiting, anorexia and mid-abdominal discomfort after a trip to the beach, where he had been allowed to roam freely.

Pertinent laboratory data included a markedly increased total calcium of 4.15mmol/L (2.15–2.95), mild azotaemia, mild neutrophilia, evidence of haemoconcentration and a borderline concentrated urine-specific gravity (1.030). Abdominal radiographs showed no evidence of a foreign body or mass effect.

Hospitalisation was initially declined, so outpatient-based conservative treatment was provided.

The patient re-presented a week later, lethargic, anorexic and trembling. The calcium was 4.48mmol/L and azotaemia and hyperphosphataemia were also present. The dog was hospitalised on intravenous fluids, antiemetics and furosemide. Advanced imaging to look for evidence of neoplasia as a potential cause of the hypercalcaemia was declined, so prednisone was also initiated.

There is no antidote and, due to lipid solubility, the elimination of a toxic dose of vitamin D may take months in some cases (Gerhard and Jaffey, 2020).

During a two-week hospital stay, additional treatments included gastrointestinal protectants, a phosphate binder and a calcium-lowering bisphosphonate drug. The hypercalcaemia and azotaemia significantly improved, but never resolved.

The dog was discharged after a second dose of bisphosphonate treatment with outpatient care. One month after the initial presentation, his hypercalcaemia and azotaemia were persistent.

Notes on vitamin D toxicity

The 25-hydroxycholecalciferol (25-OH) was >400nmol/L in each of these patients. Unfortunately a validated vitamin D assay is not available for companion animals in New Zealand and we do not have assay-specific reference intervals for vitamin D in companion animals.

However, based on the marked hypercalcaemia in each case and the high likelihood of exposure in case one, the results were expected to be elevated. This was a human assay, but cross-reaction among species is expected to be good. According to the laboratory performing the test, 25-OH vitamin D levels >200nmol/L are found in humans' vitamin D toxicity (Canterbury Health Laboratories, 2020). According to another resource, plasma concentrations of 25-OH vitamin D of 20–150nmol/L cover the normal range for most animals (Rucker et al., 2008).

The lack of hyperphosphataemia in case one called into some question the diagnosis of hypervitaminosis D, but it should be noted that not all cases are hyperphosphataemic.

Although both animals were azotaemic, the hypercalcaemia was not expected to be due to renal disease in either case, as renal disease does not tend to cause marked hypercalcaemia. In addition, vitamin D generally tends to be reduced in renal patients, not increased.

The infrequency of vitamin D toxicity means clinical suspicion may be low, and this can delay diagnosis and treatment. Without rapid and sometimes aggressive management, a massive vitamin D exposure may be deadly. Hypercalcaemia has widespread effects, including consequences for the central nervous, cardiac, gastrointestinal and renal systems.

There is no antidote and, due to lipid solubility, the elimination of a toxic dose of vitamin D may take months in some cases (Gerhard and Jaffey, 2020). Since renal and other organ system damage due to cell death and calcification may be irreversible, rapid and aggressive treatment is warranted.

This toxicity could be encountered anywhere in the country, as cholecalciferol may be used in some New Zealand cities for pest control (see **www.gw.govt.nz/cholecalciferol**) and cholecalciferol rat baits can also be bought. While secondary toxicity is fairly uncommon, it is possible, especially in animals who hunt frequently. According to Department of Conservation research, residual toxins may remain in the environment for nearly two years after bait is deployed (Thomas and Ross, 2007). While there is significant decay and non-target species are unlikely to die from exposure to an old bait, there could be significant, debilitating sub-lethal effects (Thomas and Ross, 2007). VS

These cases were seen by Sophie Bell at Vet 2 You in Whāngārei. Thanks to Sophie for her excellent case histories and diligence in working these cases up and caring for these animals.

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FURTHER READING AND REFERENCES:

Canterbury Health Laboratories. *Vitamin D*. www.labnet.health.nz/testmanager/index.php?fuseaction=main.DisplayTest&testid=1470 (accessed 17 February 2021). 2020

Crossley VJ, Bovens CP, Pineda C, Hibbert A, Finch NC. Vitamin D toxicity of dietary origin in cats fed a natural complementary kitten food. *Journal of Feline Medicine and Surgery Open Reports* 3, doi:2055116917743613. 2017

Gerhard C, Jaffey JA. Persistent increase in serum 25-hydroxyvitamin D concentration in a dog following cholecalciferol intoxication. *Frontiers in Veterinary Science* 6, 472, 2020

Rucker RB, Morris J, Fascetti AJ. Vitamins. In: Kaneko J, Harvey J, Bruss M (eds). *Clinical Biochemistry of Domestic Animals*. 6th Edtn. Pp 605–730. Academic Press, Burlington, Massachusetts, US, 2008

Thomas M, Ross P. Breakdown of cyanide and cholecalciferol in Feratox and Feracol possum baits. *DOC Research & Development Series* 288. New Zealand Department of Conservation, 2007

Zafalon RVA, Risolia LW, Pedrinelli V, Vendramini THA, Rodrigues RBA, Amaral AR, Kogika MM, Brunetto MA. Vitamin D metabolism in dogs and cats and its relation to diseases not associated with bone metabolism. *Journal of Animal Physiology and Animal Nutrition* 104, 322–42, 2020

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