Approaching the hypercalcaemic patient

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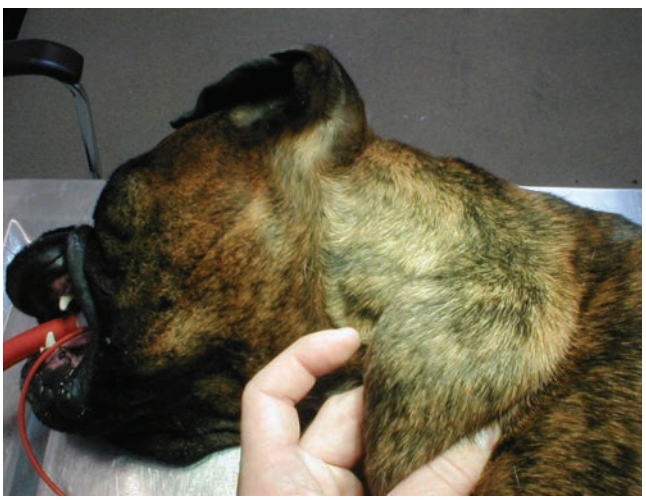

Figure 1: Enlarged left prescapular lymph node in a boxer with T-cell lymphoma. The dog had severe hypercalcaemia, leading to marked polydipsia and polyuria.

Hypercalcaemia is an uncommon electrolyte disorder in cats and dogs. Clinical signs of hypercalcaemia vary according to the severity, the speed of onset (acute versus chronic) and the underlying aetiology.

Animals may be polyuric and polydipsic, develop vomiting, anorexia, weakness and dull mentation. Signs in cats may be more subtle and they may only be lethargy and develop weight loss. When severe, hypercalcaemia can lead to irreversible damage the kidney through the deposition of calcium phosphate and cardiac function can be disrupted causing a life-threatening condition.

Common causes of hypercalcaemia in dogs are neoplastic diseases (lymphoma, anal-sac adenocarcinoma and multiple myeloma [MM]), hypoadrenocorticism, primary hyperparathyroidism and chronic renal disease (CKD).

In cats, hypercalcaemia is most often idiopathic or secondary to CKD and malignancy (lymphoma, squamous cell carcinoma SCC]). Reaching a definitive diagnosis in a patient with hypercalcaemia can be challenging, both because animals can show non-specific clinical signs and because laboratory artefacts can affect serum calcium reading.

The differentials for hypercalcaemia can be remembered with the help of the pneumonic HARDIONS. Several options are available to treat hypercalcaemia and to restore serum calcium levels within normal limits, depending on the underlying cause.

INTRODUCTION

Calcium is the most abundant element in the body due to its presence skeletal bone. It is necessary for many intracellular and extracellular functions, such as signal transmission from cell surfaces to intracellular locations, nerve conduction, neuromuscular transmission, muscle contraction, blood coagulation, hormone secretion and hepatic glycogen metabolism.

When disorders occur these can have very rapidly serious consequences for the patient, meaning logical approach to diagnosis and treatment is essential.

CALCIUM METABOLISM

Calcium homeostasis is regulated by a number of hormones the most important of which is parathyroid hormone (PTH), which is secreted by the parathyroid gland, but parathyroid hormone-related protein (PTHr-P), vitamin D and calcitonin also play a role.

Changes in serum calcium levels are detected by the Ca sensing receptor (CaSR), a G-protein present in parathyroid glands, kidneys, cartilage and bone. CaSR is activated by hypercalcaemia, reducing PTH synthesis and secretion. Conversely, hypocalcaemia inactivates CaSR increasing PTH secretion.

The primary effects of PTH are to increase serum calcium levels and decrease serum phosphate concentration via activity in three major target organs:

- **Kidneys:** PTH increases tubular absorption of calcium from the distal convoluted tubules and thick ascending loops of Henle.
- **Intestine:** PTH promotes the hydroxylation of 25(OH) vitamin D to the active form 1,25(OH) vitamin D (also called calcitriol) in the kidney. Calcitriol increases serum calcium levels mainly via the intestinal uptake, but it also allows calcium mobilisation from the bone. High concentrations of calcitriol and calcium exert negative feedback on PTH production, keeping the calcium levels in the normal range. High phosphate levels also lead to negative feedback to PTH secretion.
- **Bone:** PTH enhances calcium mobilisation from the bone by increasing the number of osteoclasts on bone surfaces.
- PTHrP is a polypeptide that can be isolated from several different organs. In normal animals, PTHrP is thought to have primarily autocrine and paracrine functions, such as lactation. It exerts the similar effects as PTH, increasing both the total and ionised calcium concentrations and decreasing phosphorus levels. Significant elevation of circulating PTHrP in the absence of lactation, are most often associated with humeral hypercalcaemia of malignancy most

Figure 2: A patient side analyser for the measurement of ionised calcium.

commonly seen with lymphoma for example (see Figure 1). Increased PTHrP levels without evidence of a malignant disease is known as humeral hypercalcemia or hypercalcaemia of benignancy (Fradkin et al, 2001) and it has been associated with benign neoplasia or granulomatous disease in humans and animals, although in veterinary literature the pathogenesis is still poorly defined. Calcitonin is a peptide synthesised by thyroid gland cells; it counteracts PTH effects limiting postprandial increases of serum Ca concentrations, but its role is relatively minor.

MEASURING CALCIUM

Extracellular calcium is present in three forms in the blood. The biologically active part is free in its ionised state, this accounts for approximately 55% of calcium present in the blood.

Around 35% of the calcium is bound to proteins, which is mainly albumin, although a smaller fraction is present bound to globulin.

The remaining 10% is complexed with anions forming compounds such as calcium bicarbonate, lactate and citrate. The percentage of calcium in each form can vary depending on protein levels acid-base balance status and on the presence of potential chelators.

Differential diagnosis for hypercalcaemia	
H	Hyperparathyroidism (primary and secondary)
A	Addison's (hypoadrenocorticism)
R	Renal failure (acute and chronic)
D	Vitamin D toxicity
I	Idiopathic (cats) or infection (granulomatous disease, eg. fungal disease)
O	Osteolysis (rare; reported with osteomyelitis and hypertrophic osteodystrophy)
N	Neoplasia (lymphoma, MM, anal-sac adenocarcinoma)
S	Spurious (lab error, excessive supplementation, etc.)

Table 1: The pneumonic HARDIONS for the diagnosis of hypercalcaemia.

An animal's serum total calcium concentration should always be interpreted with knowledge of the albumin concentration since hypoalbuminaemia can result in spurious hypocalcaemia or mask hypercalcaemia (total calcium will fall in hypoalbuminaemia, but ionised calcium will remain normal).

Changes in blood pH can lead also lead to alterations in proportion of calcium bound to proteins. In an acidotic patient, hydrogen ions are more abundant and displace calcium from blood proteins, increasing ionised calcium; the opposite happens in case of alkalosis. In both situations, the total calcium remains constant as it is only the proportion that is protein-bound that changes.

Measurement of ionised calcium should be utilised where possible and it will more accurately reflect biologically active calcium compared to the total calcium level.

Measurement of ionised calcium is not always available patient side, although a number of analysers are available to do this (see Figure 2). Samples taken for the measurement of ionised calcium need ot be carefully handles, especially if being transported for measurement. When samples are stored, red-cell metabolism increases lactic acid concentration, decreasing the pH and which can increase the ionised fraction.

Conversely, air exposure of the sample raises the pH, decreasing the ionised calcium fraction. Haemolysis and lipeamia can falsely increase measured total calcium

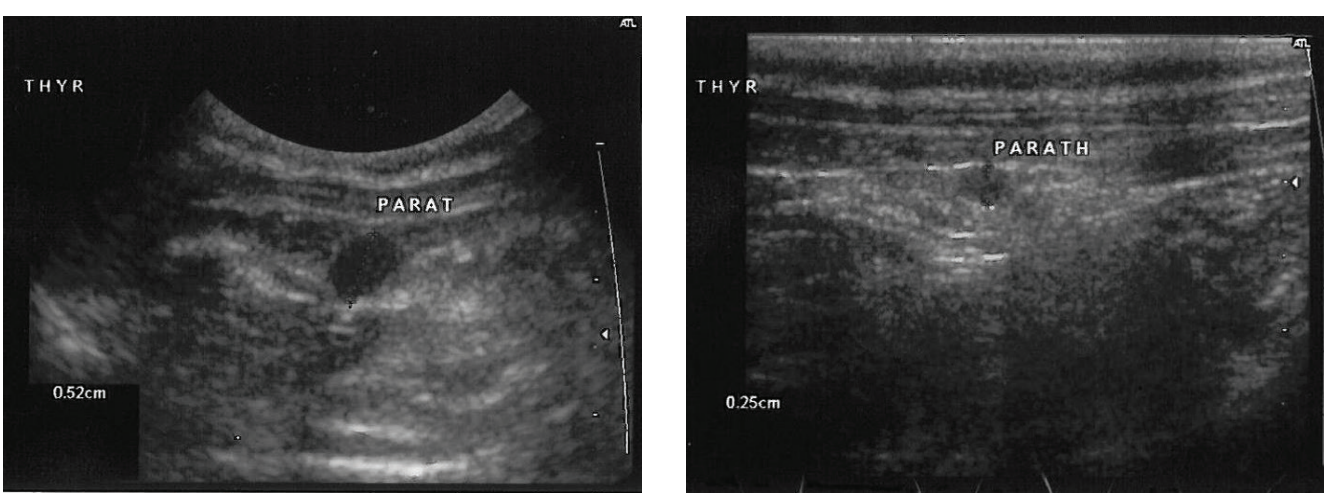

Figure 3: Ultrasound of the parathyroid glands is very useful to identify a potential active mass here the right parathyroid is normal, however the left is enlarged with a 5mm nodule.

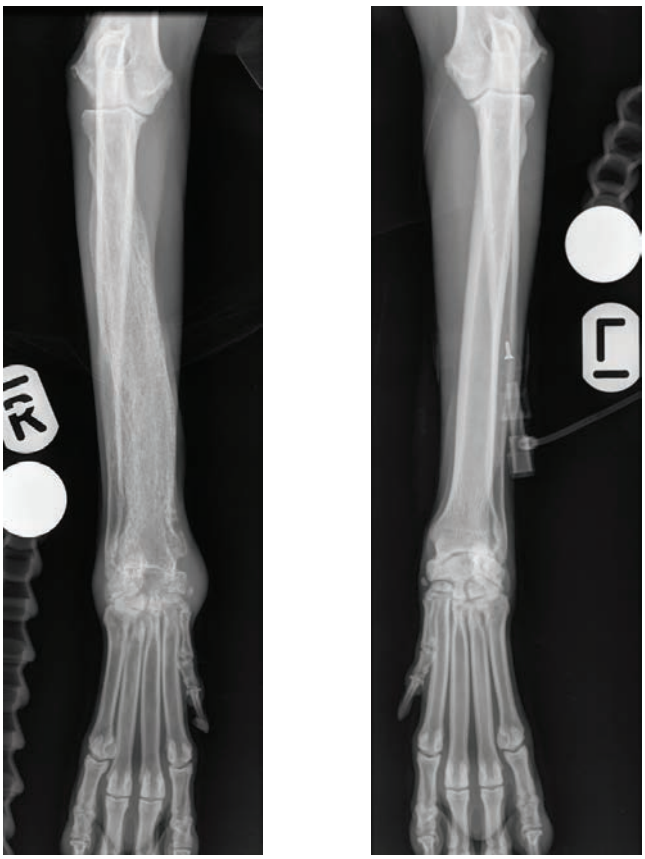

Figure 4: *Coccidioides immitis* affecting the right radius of a dog imported from Arizona, US. The dog was painful on the leg and blood tests revealed a moderate increase in calcium, which resolved and treatment for the granulomatous fungal infection was commenced.

concentrations. The anticoagulant also needs to be carefully considered with citrate, Ethylenediaminetetraacetic Acid (EDTA) and oxalate not being suitable as they chelate calcium. Serum is, therefore, typically used, although samples taken into balanced heparin will also be appropriate. The normal reference intervals for ionised calcium vary between analyser and anticoagulant used but is usually reported as between 1.1mmol/l and 1.4mmol/l.

WHAT CAUSES HYPERCALCAEMIA?

Hypercalcaemia is usually associated with total calcium concentrations greater than 3mmol/l and ionised calcium greater than 1.5mmol/L. The differentials for hypercalcaemia can be remembered with the help of the pneumonic HARDIONS (see Table 1). The most common cause of hypercalcaemia in an older dog is malignancy, either through elevation in PTHrp or excessive osteolysis. Lymphoma (usually T-cell in origin), anal-sac adenocarcinoma and MM are the most common causes of malignancy-related hypercalcemia in dogs. Other common causes are hypoadrenocorticism, primary hyperparathyroidism and chronic renal disease (CKD).

Primary hyperparathyroidism is a well-recognised cause of hypercalcaemia in older dogs. It usually develops in presence of a solitary adenoma, carcinoma or adenomatous hyperplasia of one parathyroid gland which leads to an excessive secretion of PTH, although multiple glands can be affected (see Figure 3). Increased PTH levels are also found in cats and dogs in later stages of CKD, developing secondary hyperparathyroidism. Animals with CKD typically have azotaemia, normal to low calcium levels with hyperphosphatemia, and isostenuria. However, a small proportion of animals with CKD become hypercalcaemic; in this case the aetiology is poorly understood. Approximately 30% of dogs diagnosed with Addison's disease are hypercalcaemic; the underlying mechanism remains still unknown (Ettinger et al, 2017).

In cats the most common causes of hypercalcaemia are idiopathic (IHC), CKD and malignancy-related. SCC, mostly of the head and neck, has been reported as frequently as lymphoma as a cause of hypercalcaemia of malignancy (de Brito Galvão et al, 2017). Anal-sac adenocarcinomas are very rare in cats. At this time, the underlying mechanism of IHC are unknown, but increased bone resorption has been hypothesised as a cause or important component (Hardy et al, 2015). The diagnosis is one of exclusion.

Hypervitaminosis D is a rare cause of hypercalcaemia in dogs and cats, but important to consider during investigations. In dogs, toxicity has been reported following accidental ingestion of petroleum-based antipsoriasis ointments containing calcipotriene, a synthetic vitamin D3 analogue. A dose of 40g to 60g of calcipotriene per kilogram of body weight can cause severe hypercalcaemia and has a significant risk of mortality (Saedi et al, 2007). Hypervitaminosis D can also follow ingestion of rodenticides containing cholecalciferol, overzealous dietary supplementation (Wehner et al, 2013) or during vitamin D treatment of hypoparathyroidism. Therefore, it is important to know from the history if the hypercalcemic patient has been previously exposed to toxins, plants or drugs and measuring blood 25-OH-vitamin D levels can help exclude hypervitaminosis D as a possible cause.

Granulomatous diseases, such as schistosomiasis, histoplasmosis, blastomycosis and coccidioidomycosis (see Figure 4), nocardiosis, atypical mycobacteria, aspergillosis and *Angiostrongylus vasorum* (see Figure 5) infections have been reported as a rare cause of hypercalcaemia in dogs. While, in human medicine, the association between hypercalcaemia and granulomatous diseases has been well-defined, in veterinary medicine the underlying pathogenetic mechanism is still unclear. It has been proposed to be likely an excessive production of 1,25-(OH)2-vitamin D by activated macrophages within the granulomatous inflammation (Mellanby et al, 2006), although it is not been reported in all cases. Granulomatous inflammation is also been associated to increased synthesis of PTHrP (Fradkin et al, 2001).

Osteolytic processes causing hypercalcaemia are rarely reported and are secondary to malignant neoplasia (osteosarcoma and metastatic bone tumours), osteomyelitis or hypertrophic osteodystrophy.

WHAT ARE THE CLINICAL SIGNS OF HYPERCALCAEMIA?

Clinical signs of hypercalcaemia vary according to the

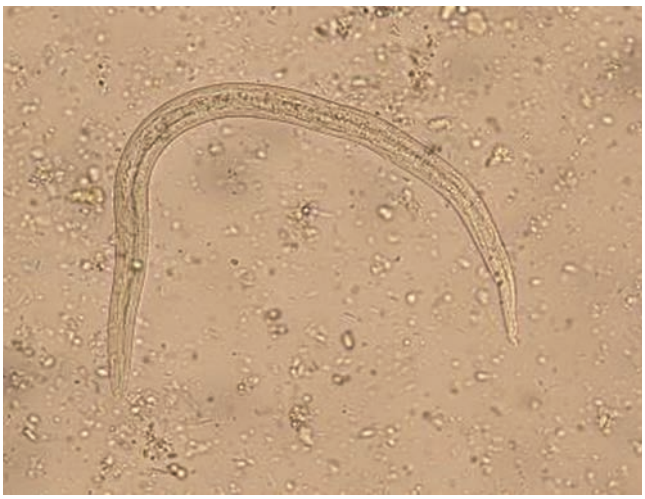

Figure 5: An *Angiostrongylus vasorum* L1 larvae recovered from a rectal scrape of a dog presenting with a cough and mild hypercalcaemia.

severity, the speed of development (acute versus chronic) and the underlying aetiology. Increased serum calcium concentrations inhibit the action of anti-diuretic hormone (ADH) in the kidney leading to secondary diabetes insipidus; this leads to primary polyuria and secondary polydipsia. Dehydration and prerenal azotemia occur secondary to gastrointestinal losses and polyuria. Renal vasoconstriction, tubular necrosis and interstitial fibrosis can result in renal failure which can lead to death.

Other clinical signs of hypercalcaemia are vague and non-specific these include weakness, vomiting and dull mentation. Anorexia may be due to direct effects of calcium on the central nervous system (CNS) or to decreased excitability of smooth muscle cells in the gastrointestinal tract.

Weakness can occur as high calcium levels decrease excitability of skeletal muscles; listlessness and depression occurs from the direct effects of hypercalcaemia on the CNS. Hypercalcaemia increases the likelihood of calcium uroliths and urinary tract infection (Sakals et al, 2010). Cats do not exhibit polyuria, polydipsia, or vomiting as often as dogs.

Cats with idiopathic hypercalcaemia (IHC) typically have weight loss and lethargy; some cats, however, may have no clinical signs and the hypercalcaemia is found as an incidental finding. The presence of lower urinary tract signs can also be recognised in some cats and may be indicative of urolithiasis. Less common, but potentially fatal complications in both species include obtundation, seizures, coma and arrhythmias. Although uncommonly reported, arrhythmias are thought to be a direct consequence of dystrophic mineralisation of the myocardium. Gastrointestinal effects can be secondary to reduction in intestinal smooth muscle contractility and gastric ulceration via direct stimulation of the parietal cells to produce gastrin.

When ionised hypercalcaemia is present, serum phosphorus levels must be closely monitored because concomitant elevations in those minerals have been reported to cause soft-tissue mineralisation. Multiplication of the total serum calcium (mmol/l) by the serum phosphorus (mmol/l) yields the calcium-phosphorus product. Growing animals have a normal product of >7. In adult animals, a calcium-phosphorus product of >6-7 has been reported to increase the risk of soft-tissue mineralisation. Usually clinical signs become evident when the kidneys or cardiac structures undergo mineralisation, with irreversible damage.

DIAGNOSIS

A correct diagnostic approach to hypercalcaemia starts obtaining a thorough history that will indicate the likelihood of vitamin D toxicosis owing to excessive supplementation, rodenticide, certain plants (eg. *Trisetum flavescens*, *Solanum malacoxylon* or *Cestrum diurnum*) or anti-psoriasis creams. A complete physical examination (including a careful rectal examination) is fundamental to assess the size of peripheral lymph nodes, to exclude the presence of rectal masses or any other palpable mass and to identify any skeletal pain.

Diagnostic work-up for hypercalcaemia should include a minimum database of complete blood count, serum biochemistry, ionised calcium and blood stored for the later measurement of PTH/PTHrp and vitamin D. Urinalysis should be performed in order to assess the renal function; sediment examination can reveal signs of low urinary tract infections. Once established that ionised calcium is definitely increased and that this is persistent, further tests can be carried out to systematically rule out many causes of hypercalcaemia and to try reaching a definitive diagnosis. In case of increased serum total calcium levels is important to measure ionised calcium levels to confirm the suspect of a true hypercalcaemia, avoiding as much as possible any laboratory artefacts. In most hypercalcaemic patients, ionised calcium will represent approximately 55% of the total calcium; however, in renal failure the ionised component is often lower than would be expected when compared to the total. In fact, animals with CKD usually have normal to low ionised calcium, with concurrent hyperphosphatemia.

However, it is important to remember that a small proportion of cats and dogs with CKD become hypercalcaemic. In cats, it has been recommended measuring ionised calcium as well as a total calcium because of the lack of concordance between the two. It has been shown that approximately 64% of cats with ionised hypercalcaemia had normal total calcium (de Brito Galvão et al, 2017).

When appropriate, basal cortisol and an adrenocorticotropic hormone (ACTH)-stimulation test should be considered to exclude hypoadrenocorticism (Addison's disease) in dogs. PTH levels measurement is helpful to detect if the hypercalcemia is parathyroid-dependent or not. In case of primary hyperparathyroidism and CKD, PTH levels can be normal or increased and in both cases the PTH is in appropriate for the higher than normal level of calcium present. In case of parathyroid-independent diseases the production of

PTH is physiologically suppressed by the high serum calcium levels, as during malignancy and hypervitaminosis D. It is usually within normal ranges in animals with hypoadrenocorticism. An extended database may include determination of serum 25-hydroxyvitamin D, 24,25(OH)2-vitamin D, calcitriol, and parathyroid hormone-related protein (PTHrP) concentrations. In cats, the measurement of plasma PTHrP is not as useful as it is in dogs, because it is often negative.

When PTHrP is positive, malignancy is most likely. In cats the reference range for vitamin D is wide and has been established in cats already consuming diets containing vitamin D. Therefore, in cats with IHC the concentration of 25-hydroxyvitamin D and calcitriol are most often within the reference range, but this does not necessarily exclude toxicity (de Brito Galvão et al, 2017).

To exclude neoplasia, thoracic radiographs and abdominal ultrasound should be performed.

The purpose for the radiographic study is to assess the cranial mediastinum for a mass consistent with lymphoma or thymoma. If present, fine-needle aspiration or tissue biopsy should be considered.

Radiographs are also useful to evaluate the peri hilar area and lungs for neoplasia or systemic mycoses, the spine and ribs for lytic lesions caused by neoplasia. An abdominal ultrasound allows the clinician to assess the size and consistency of the liver, spleen and mesenteric and sublumbar lymph nodes for abnormalities suggestive of malignancy (lymphoma) or other conditions.

When possible, abnormal areas should be aspirated or biopsied to help ruling out the presence of neoplasia. The size and consistency of the kidneys can be assessed; the bladder should be evaluated for the presence of cystic calculi.

Fine needle aspirates of the lymph nodes should be performed when enlarged, or in case of suspect of lymphoma, together with a bone-marrow biopsy when appropriate.

Ultrasonography of the neck region has become very sensitive in detecting enlarged parathyroid glands, generally those that are 2mm or larger, or to localise parathyroid masses. Nuclear scintigraphy has been used to attempt identification of hyper-functioning parathyroid glands, but its accuracy was found to be poor, so it is not recommended in animals. To have a definitive diagnosis of an enlarged parathyroid gland, histopathology should be performed on an excised gland.

In animals that have history of travel and apparently an unknown cause for hypercalcaemia, a faecal examination is recommended to rule out parasitic diseases (Rohrer et al, 2000).

TREATMENT

Treatment for hypercalcaemia is aimed at treating the underlying cause, promoting calcium excretion, decreasing bone and intestinal calcium resorption and promoting extravascular calcium shift.

First-line treatment to stabilise the critical hypercalcaemic patient is commencing intravenous fluid therapy with 0.9% sodium chloride, this restores circulating fluid volume and encourages diuresis.

The effect of the increased sodium concentration on the kidney is increasing the glomerular filtration rate as well as competitive inhibition of tubular calcium reabsorption.

It is important to monitor the animal for any sign of over-hydration and to check sodium levels to avoid inducing hypernatraemia.

Once the fluid resuscitation is complete and the patient is well hydrated, frusemide can be given (0.5-2mg/kg i/v) to promote increased renal excretion (calciuria). Although frusemide can increase calcium excretion by over 50 times, care needs to be taken to replace all fluids lost as a result of the increased diuresis, to avoid haemoconcentration and hypokalaemia.

The one off bolus can be followed by intermittent frusemide treatment or a constant rate infusion (suggested dosage 0.5mg/kg/hour). A recent study revealed that constant rate infusion administration leads to better diuresis and calciuresis compared to bolus therapy (Adin et al, 2003).

Sodium bicarbonate (1-4mmol/kg slow i/v or at a constant rate infusion) can be used in the management of an acute hypercalcaemic crisis, as producing an alkalosis status which increases calcium binding to protein, thus reducing ionised calcium serum levels.

It is useful in combination therapy, especially when metabolic acidosis is present. However, care needs to be taken when giving bicarbonate as over treating can lead to a metabolic alkalosis, which is hard for the body to resolve. As a result, bicarbonate is usually only given after other treatments or in severely acidotic patients.

The use of glucocorticoids can be beneficial in the treatment of certain causes of hypercalcaemia, enhancing calcium renal excretion and reducing intestinal uptake. In the bone, steroids act by inhibiting osteoclast maturation and therefore bone resorption; they also diminish calcitriol receptors present in the bone.

Vitamin D antagonism has also been observed with glucocorticoids. It is essential that steroids are only used once a definitive diagnosis is made, as further diagnostic tests will be affected by the administration of steroid therapy and to start using the lowest dose possible (ie. prednisolone: 1-2mg/kg/day).

Bisphosphonates are frequently used to treat hypercalcaemia as they decrease serum calcium levels by inhibition of osteoclastic activity and induction of apoptosis. They have also been reported to interfere with the intestinal absorption of calcium.

Being fully effective 24-48 hours after parenteral administration, bisphosphonates are not considered initial drugs of choice for acute therapy; they are used if the hypercalcaemia is expected to be protracted or if calcium is determined to be from bony origin.

Pamidronate is the most used bisphosphonate; it is absorbed by the bone by 50-60% after intravenous administration and it is excreted unchanged by the kidneys. Its use is very safe in humans and animals if the

recommended doses are respected. It can be administered intravenously as an infusion with 0.9% sodium chloride over 24 hours (at the dosage of 0.9-1.3mg/kg for dogs, 1.5-2mg/kg for cats). Zoledronate can be used intravenously at the dosage of 0.1-0.2 mg/kg over 30-60 minutes. Administration of bisphosphonates can be repeated every two to four weeks if needed and oral bisphosphonates can then be considered for maintenance therapy.

In cats, current recommendations for the management of IHC and often concurrent calcium oxalate urolithiasis include a diet change to a non-acidifying, high-fibre diet to decrease calcium absorption from the gastrointestinal tract, in combination with medical treatments such as prednisolone and bisphosphonates.

Response to one or a combination of these treatments has been successful in some cases, but response is unpredictable and often transient.

In a recent study (Hardy et al, 2015), it has been proposed the use of the oral bisphosphonate alendronate for the treatment of IHC in cats, which was well tolerated and was successful in decreasing ionised calcium concentrations in most cats without clinically apparent adverse effects during six months of treatment.

Calcitonin can decrease very rapidly serum calcium concentration by inhibiting the synthesis and activity of osteoclasts in the bone. It is very useful, in case the cause of hypercalcaemia is still unknown, but at the same time it is required to decrease quickly serum calcium levels.

The disadvantages are that calcitonin is quite expensive, it has a short lived effect (hours), resistance to treatment can develop after 12-24 hours and that the response of the patient is unpredictable.

Side effects that have been documented in animals are vomiting, diarrhoea and allergic reactions.

In case of primary hyperparathyroidism, the treatment of choice is removal of the parathyroid masses.

Surgical intervention can be performed, followed by histopathology on the tissue to confirm the definitive diagnosis (although in case of neoplasia, very often it can be difficult to histologically distinguish between parathyroid adenoma and carcinoma).

Alternative therapies that have been reported include chemical ablation of the affected glands and percutaneous ultrasound-guided radiofrequency thermoablation.

Postoperatively, it is important to monitor the patient for hypocalcaemia, which commonly develops one to six days after surgery.

Treatment with calcitriol and vitamin D supplements can be instituted to help keeping serum calcium level within normal ranges. If renal failure doesn't develop secondary to hypercalcaemia, the long-term prognosis after removal of a parathyroid tumour is excellent (Bonagura et al, 2009).

CASE STUDY

A 13-year-old, female, neutered Border terrier presented for further evaluation of PU/PD and lethargy, which had progressed over the two months prior to presentation.

Investigation prior to referral had revealed a moderate hypercalcaemia and but no other findings were present on imaging (chest and abdominal radiographs).

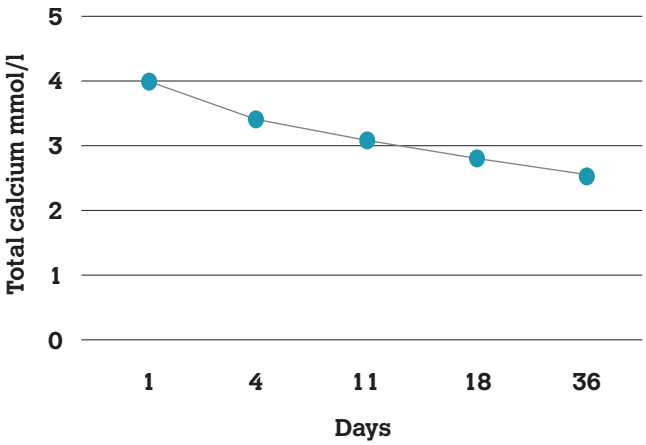

Figure 6.

At presentation, the dog was bright and alert and in good body condition.

Clinical examination revealed marked gingivitis, but was otherwise unremarkable. Peripheral lymph nodes were a normal size and both anal glands were normal on rectal examination. The dog was admitted and blood samples were taken.

Haematology revealed a mild neutrophilia (12.2x10^9/l, reference interval 3-11.5x10^9/l) which felt to be due to the gingivitis. Biochemistry revealed a marked hypercalcemia (total calcium 4.04mmol/l, reference interval 2.3-3mmol/l) but was otherwise unremarkable. Ionised calcium was moderately increased (1.68mmol/l, reference interval 1.1-1.4mmol/l).

Serum phosphate levels were at the low end of the normal range (0.85mmol/l, reference range 0.6-1.4mmol/l) giving a calcium-phosphate product of 3.43; values above six are of a concern as at this level calcium phosphate will precipitate within tissues, which in the long term will compromise renal function.

In this case, the most likely differential for hypercalcemia is neoplasia with lymphoma, anal-sac carcinoma and MM.

Renal failure is unlikely in the basis of the biochemistry and elevated ionised calcium, however, full assessment of renal-concentrating ability is not possible due to hypercalcaemia interfering with the action of ADH leading to PU/PD through secondary nephrogenic diabetes insipidus (the dog's urine-specific gravity [USG] was 1.014).

Addison's is also unlikely on the basis of the serum biochemistry.

To investigate, further blood was submitted for the determination of PTH and PTHrp.

These results returned to reveal that the PTH was markedly elevated (470pg/ml, reference interval 18-130pg/ml) with very low levels of PTHrp (0.95pmol/l, >2pmol/l suggestive of malignancy).

These results suggested the presence of primary hyperparathyroidism and cervical ultrasound was performed; this revealed the presence of a large mass in

left parathyroid gland (5.2mm in diameter) confirming the diagnosis (see Figure 3). Given the marked hypercalcaemia, aggressive saline diuresis was commenced (3 x maintenance 0.9% sodium chloride) and over the course of 48 hours, the total calcium fell to 3.42mmol/l.

At this point, definitive treatment was discussed with the owner. Surgical removal of the parathyroid gland is the treatment of choice for hyperparathyroidism; however the owner was concerned about the risks of anaesthesia and had financial constraints.

The alternative of percutaneous ultrasound-guided ethanol ablation was discussed and informed consent was obtained. Under general anaesthesia the parathyroid nodule was identified and the cervical region clipped and aseptically prepared.

The approximate volume of the nodule was calculated and an equal volume of ethanol (0.05ml) was injected into the nodule using ultrasound guidance and a 27g needle.

The dog recovered well from the procedure, however, 24 hours later, transient signs of laryngeal paralysis were noted, with inspirtory stridor and slight dyspnoea.

These signs abated quickly and were thought to be due to direct local irritation of the recurrent laryngeal nerve which runs in close proximity to the parathyroid with the vagosympathic trunk. Serum calcium was closely monitored and over the course of the next 10 days returned to normal.

Vitamin D was not given post-procedure as serum calcium was <3.5mol/l. However, it would have been instigated had hypocalcaemia been documented.

At follow-up, six months later, the dog was clinically normal.

Ethanol ablation represents an efficacious alternative to surgical parathyroidectomy, with this procedure leading to a good clinical and cost-efficient outcome.

Long et al, 1999, reported a series of 12 dogs, of which 11 were clinically cured after a single injection of ethanol at 18 months follow-up.

One dog needed a repeat injection and two dogs suffered transient laryngeal paralysis as seen in this patient.

CONCLUSION

If there is a logical progression through the differential diagnosis for hypercalcaemia, the diagnostic pathway can be very rewarding.

While there are a number of potential malignancies, these have treatment options and there are a number of possible non-malignant cases that can lead to excellent long-term outcomes with appropriate management.

REFERENCES ON REQUEST

READER QUESTIONS AND ANSWERS

1: WHICH OF THE FOLLOWING STATEMENTS IS CORRECT?

- **A** Total calcium will be lower in dogs with hypoalbuminaemia
- **B** Ionised calcium will be elevated in dogs with hyperglobulinaemia
- **C** Total calcium will be increase in acidotic animals
- **D** Ionised calcium is stable for several days before measurement in whole blood

2: WHICH OF THE FOLLOWING STATEMENTS IS INCORRECT?

- **A** Hypoadrenocorticism is an uncommon cause of hypercalcaemia
- **B** Anal sac adenocarcinoma is very rare in cats
- **C** Laboratory errors can occur by using the wrong anticoagulant
- **D** B-cell lymphoma is the most common cause of hypercalcaemia in dogs

3: WHICH OF THE FOLLOWING STATEMENTS ABOUT TREATING HYPERCALCAEMIA IS CORRECT?

- **A** Steroid treatment increases calcium excretion in the kidney
- **B** Frusemide is less effective at reducing calcium levels as a chronic renal insufficiency (CRI) compared to bolus therapy
- **C** Steroids should only be given after all diagnostic test are completed as they may prevent a diagnosis from being achieved
- **D** Bisphosphonates can be given orally in an emergency to rapidly reduce serum calcium levels

4: FRUSEMIDE INCREASES CALCIUM EXCRETION IN THE KIDNEY BY?

- **A** 0.5 times normal
- **B** 5 times normal
- **C** 50 times normal
- **D** 500 times normal

5: WHICH OF THE FOLLOWING STATEMENTS REGARDING PTH IS INCORRECT?

- **A** PTH is unstable and samples should be separated and frozen immediately
- **B** Measurement of PTH can easily be performed patient side
- **C** PTH is produced in the parathyroid gland
- **D** PTH leads to calcium resorption in the distal convoluted tubule

ANSWERS: 1:A; 2:D; 3:C; 4:C; 5:B