Hypercalcaemia in a dog with primary hypothyroidism

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ABSTRACT
A 7-year old female beagle was evaluated for symptomatic hypercalcaemia and primary hypothyroidism. Clinical findings were typical for hypothyroidism. Plasma parathyroid hormone was low and obvious causes for the hypercalcaemia were ruled out by means of abdominal ultrasonography, ultrasonography of the parathyroid glands, survey thoracic radiographs, and fine needle aspirate cytology of the spleen, liver, and peripheral lymph nodes. Treatment with thyroxine resulted in resolution of the hypercalcaemia after approximately 9 weeks of therapy. This is the 1st report of primary adult-onset hypothyroidism associated with symptomatic hypercalcaemia in a dog.

Keywords: calcium, canine, total T4, TSH.


INTRODUCTION
Hypercalcaemia is not an unusual problem in dogs, with common causes being lymphoma, hypoadrenocorticism, primary hyperparathyroidism and chronic renal failure. Less common causes are anal gland adenocarcinoma, multiple myeloma, and vitamin D toxicosis; with rare causes being carcinomas of the lung, mammary gland, nasal passage, pancreas, testicle, thymus, thyroid and vagina, acute renal failure, nutritional, and granulomatous disease.

The major cause of acquired hypothyroidism in the dog is lymphocytic thyroiditis or idiopathic thyroid atrophy, resulting in a decreased production of triiodothyronine (T3) and thyroxine (T4) by the thyroid gland and referred to as primary hypothyroidism. A less common cause is dysfunction of either the pituitary gland or hypothalamus, referred to as secondary and tertiary hypothyroidism respectively.

Clinical signs of hypothyroidism may be nonspecific and insidious in onset. Common clinical signs include lethargy, mental dullness, weight gain, unwillingness to exercise, cold intolerance, dermatopathies, and sinus bradycardia. Common laboratory changes associated with hypothyroidism are mild non-regenerative anaemia and fasting hypercholesterolaemia and hypertriglyceridaemia. Less common and less specific abnormalities are mild increases in alkaline phosphatase (ALP) and alanine aminotransferase (ALT) activity, and creatine kinase.

Mild hypercalcaemia has only been reported in dogs with congenital hypothyroidism, with the proposed mechanism being decreased renal clearance and/or increased gastrointestinal absorption of calcium. Untreated hypothyroid puppies continue to show mildly elevated serum calcium levels during adulthood.

This article reports a case of primary adult-onset hypothyroidism in a beagle associated with symptomatic hypercalcaemia.

CASE HISTORY
A 7-year old neutered female beagle was referred for evaluation of hypercalcaemia (3.27, reference interval 2–3 mmol/l) and recently diagnosed primary hypothyroidism. The diagnosis of hypothyroidism was based on subnormal total T4 (<6, reference interval 18–45 nmol/l) and elevated thyroid stimulating hormone (TSH) 1.05 (reference interval 0.02–0.8 ng/ml). Pertinent history was the presence of polyuria and polydipsia (PuPd), poor appetite, and weight gain. Abnormalities on clinical examination were obesity, bradycardia (heart rate of 80 beats per minute) and a firm mass on the perineum, which on fine needle aspirate cytology was consistent with a lipoma. Rectal palpation was within normal limits. The only pertinent finding on urine analysis was an inappropriate urine specific gravity (1.018). On serum biochemistry analysis hypercholesterolaemia (13.5, reference interval 3–6 mmol/l) and hypercalcaemia (3.44 mmol/l) were present whereas serum urea, creatinine, total proteins, albumin, globulin, sodium, potassium, and liver enzyme activity were all within normal limits. No abnormalities were evident on complete blood count, abdominal ultrasonography, ultrasonography of the parathyroid glands, survey thoracic radiographs and fine needle aspirate cytology of the spleen, liver and peripheral lymph nodes. Plasma parathyroid hormone (PTH) was low (7, reference interval 15–25 pg/ml). Renal fractional clearance of calcium was 0 (reference interval 0–0.4). The dog was treated with 300 µg thyroxine sodium twice a day – 0.024 mg/kg per day (Eltroxin, GlaxoSmithKline, Sloane Street, Bryanston, South Africa) and on follow up assessment 2 weeks later the dog was more active, the bradycardia had resolved, but the PuPd was still present. Serum calcium was still elevated (3.46 mmol/l). Thyroxine was continued at 300 µg twice a day. On follow up assessment 9 weeks later the dog was active, had lost weight, and the PuPd had resolved. Both serum calcium and total T4 had normalised; 2.97 mmol/l and 25.5 nmol/l, respectively. Repeat assessments showed ongoing weight loss and no PuPd. Fifteen months after the initial diagnosis, body weight was stable, activity normal, PuPd was not present, and serum calcium total T4, TSH, an PTH were all within reference range (2.93 mmol/l, 32 nmol/l, 0.11 ng/ml, and 20 pg/ml, respectively).

DISCUSSION
The dog in this report had primary acquired hypothyroidism – typical clinical signs, low total T4, and high TSH together with unexplained hypercalcaemia. Hypercalcaemia, secondary to a variety of conditions, is diagnosed relatively frequently in dogs, with the most common cause being malignancy-associated hypercalcaemia, such as lymphoma, anal gland adenocarcinoma, multiple myeloma and various other organ carcinomas. None of these conditions were present at either initial or subsequent evaluations and furthermore, 15 months after the initial diagnosis, the
after thyroxine replacement therapy, which is similar to the dog in this report. Hypercalcaemia is often associated with hyperthyroidism in humans and can occur in as many as 47% of hyperthyroid patients, with decreased PTH concentrations noted in most hyperthyroid patients suggesting a parathyroid-independent hypercalcaemia. As the dog in this report had hypercalcaemia with low PTH concentration it would also suggest parathyroid-independent hypercalcaemia. In hyperthyroid people, calcitriol concentration is typically decreased, most likely because of a decrease in intestinal 1α-hydroxylase activity secondary to the hypercalcaemia and PTH suppression. Decrease in calcitriol concentration may account for the decrease in intestinal calcium absorption that has been noted in hyperthyroidism, even though thyroid hormone concentrations can stimulate calcium absorption. Calcitriol concentrations were not determined in this dog. Hyperthyroidism in people is not characterised by significant changes in calcium homeostasis; however, treatment of hyperthyroidism may cause an increase in bone turnover with a loss in bone mineral density.

Thyrotoxicosis is quite often accompanied by hypercalcaemia in either humans or animals. Although a sudden lymphoplasmacytic inflammation of the thyroid glands can result in transient thyrotoxicosis, the dog in this report had long-standing clinical signs of hyperthyroidism and thus a thyrotoxicosis could be ruled out.

In conclusion the only logical explanation for the cause of the hypercalcaemia in this dog would be hyperthyroidism, as no other aetiology was discovered. The hypercalcaemia resolved with thyroxine therapy, and the PTH normalised.

REFERENCES