Hypercalcaemia in a dog with primary hypothyroidism

R G Lobetti[a]

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.

Lobetti R G **Hypercalcaemia in a dog with primary hypothyroidism**. *Journal of the South African Veterinary Association* (2011) 82(4): 242–243 (En.). Bryanston Veterinary Hospital, PO Box 67092, Bryanston, 2021 South Africa.

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[3].

The major cause of acquired hypothyroidism in the dog is lymphocytic thyroiditis or idiopathic thyroid atrophy[11], resulting in a decreased production of triiodothyronine (T_3) and thyroxine (T_4) 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[11]. 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[8,11]. 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[11].

Mild hypercalcaemia has only been reported in dogs with congenital hypothyroidism[4,5], with the proposed mechanism being decreased renal clearance and/or increased gastrointestinal absorption of calcium[5]. Untreated hypothyroid puppies continue to show mildly elevated serum calcium levels during adulthood[4].

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[3]. None of these conditions were present at either initial or subsequent evaluations and furthermore, 15 months after the initial diagnosis, the

[a]Bryanston Veterinary Hospital, PO Box 67092, Bryanston, 2021 South Africa.
E-mail: rlobetti@mweb.co.za

Received: July 2011. Accepted: November 2011.

dog did not show any signs of obvious neoplasia. As the neoplasms associated with hypercalcaemia are malignant, it would be highly unlikely that they would remain clinically silent for such a long period. Other causes of hypercalcaemia that were excluded included hypoadrenocorticism (normal electrolytes and no clinical signs over an extended follow-up period), primary hyperparathyroidism (low PTH), acute and chronic renal failure (normal urea and creatinine), vitamin D toxicosis (no history), nutritional (normal diet), and granulomatous disease (normal radiographs and ultrasonographic examinations)[3].

Little is known about the effects of thyroid disorders on calcium metabolism in dogs[10]. In humans with adult-onset hypothyroidism serum concentrations of calcium and phosphorus are typically within normal limits[7], whereas in congenital hypothyroidism up to 23 % of children exhibit hypercalcaemia with elevated concentrations of PTH and calcitriol[8]. Mild hypercalcaemia (up to 3.04 mmol/ℓ) has been reported in dogs with congenital hypothyroidism[4,5], with untreated puppies continuing to show mildly elevated serum calcium levels during adulthood[4]. The proposed mechanism for the hypercalcaemia is decreased renal clearance and/or increased gastrointestinal absorption of calcium[5]. The dog in this report had markedly elevated serum calcium levels together with what would appear to be a compensatory low PTH. In addition the renal fractional clearance of calcium was zero, which could imply decreased renal clearance. In this dog, as the hypothyroidism only developed at around the age of 7 years, congenital hypothyroidism could be excluded. In children with congenital hypothyroidism hypercalcaemia is transient and reversible after thyroxine replacement therapy[12], 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[2], with decreased PTH concentration 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[1], most likely because of a decrease in renal 1a-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[6], even though thyroid hormone concentrations can stimulate calcium absorption. Calcitriol concentrations were not determined in this dog. Hypothyroidism in people is not characterised by significant changes in calcium homeostasis; however, treatment of hypothyroidism may cause an increase in bone turnover with a loss in bone mineral density[10].

Thyrotoxicosis is quite often accompanied by hypercalcaemia in either humans or animals[9]. Although a sudden lymphoplasmacytic inflammation of the thyroid glands can result in transient thyrotoxicosis[11], the dog in this report had long-standing clinical signs of hypothyroidism 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 hypothyroidism, as no other aetiology was discovered, the hypercalcaemia resolved with thyroxine therapy, and the PTH normalised.

REFERENCES

1. Auwerx J, Bouillon R 1986 Mineral and bone metabolism in thyroid disease: a review. *Quarterly Journal of Medicine* 60: 737–752
2. Begic-Karup S, Wagner B, Raber W, Schneider B, Hamwi A, Waldhäusl W, Vierhapper H 2001 Serum calcium in thyroid disease. *Wiener Klinische Wochenschrift* 113: 65–68
3. Feldman E C 2010 Disorders of the parathyroid glands. In Ettinger S J, Feldman E C (eds), *Textbook of veterinary internal medicine* (7th edn). Saunders Elsevier, St Louis: 1722–1750
4. Greco D S, Peterson M E, Cho D Y, Markovitis J E 1985 Juvenile-onset hypothyroidism in a dog. *Journal of the American Medical Veterinary Association* 187: 948–950
5. Greco D S, Feldman E C, Peterson M E, Turner J L, Hodges C M, Shipman W 1991 Congenital hypothyroid dwarfism in a family of giant schnauzers. *Journal of Veterinary Internal Medicine* 5: 57–65
6. Haldimann B, Kaptein E M, Singer F R, Nicoloff J T, Massry S G 1980 Intestinal calcium absorption in patients with hyperthyroidism. *Journal of Clinical Endocrinology and Metabolism* 51: 995–997
7. Kisakol G, Kaya A, Gonen S, Tunc R 2003 Bone and calcium metabolism in subclinical autoimmune hyperthyroidism and hypothyroidism. *Endocrine Journal* 50: 657–61
8. Panciera D L 1994 Hypothyroidism in dogs: 66 cases (1987–1992). *Journal of the American Veterinary Medical Association* 204: 761–767
9. Pérez A V, Picotto G, Carpentieri A R, Rivoira M A, Peralta López M E, Tolosa de Talamoni N G 2008 Mini-review on regulation of intestinal calcium absorption *Digestion* 77: 22–34
10. Schenck P A 2007 Calcium homeostasis in thyroid disease in dogs and cats. *Veterinary Clinics of North America: Small Animal Practice* 37: 693–708
11. Scott-Moncrieff J C 2010 Hypothyroidism. In Ettinger S J, Feldman E C (eds) *Textbook of veterinary internal medicine* (7th edn). Saunders Elsevier, St Louis: 1722–1750
12. Verrotti A, Greco R, Altobelli E, Morgese G, Chiarelli F 1998 Bone metabolism in children with congenital hypothyroidism – a longitudinal study. *Journal of Pediatric Endocrinology and Metabolism* 11: 699–705