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Voedselgerelateerde hyperthyroïdie bij een rottweiler

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ABSTRACT

In this report, a clinical case of dietary hyperthyroidism in a dog is described. An eleven-month-old, male intact Rottweiler was presented because of panting, weight loss and increased serum total thyroxine concentration. A complete history revealed that the dog was fed a bone and raw food diet, which made dietary induced hyperthyroidism very likely. Other possible differentials were excluded after a thorough diagnostic work-up. Finally, after changing towards a traditional commercial maintenance diet, the clinical symptoms resolved and thyroid blood values normalized. In every dog with an increased serum total thyroxine concentration, with or without clinical signs of hyperthyroidism, a thorough dietary history should be obtained. Owners should be informed that raw food diets tend to be nutritionally imbalanced, carry the risk of bacterial contamination, and have other safety problems. Therefore, veterinarians should recommend against feeding these diets.

SAMENVATTING

In deze casuïstiek wordt een geval van voedselafhankelijke hyperthyroïdie bij een hond beschreven. Een mannelijke, intacte rottweiler van elf maanden oud werd aangeboden omwille van hijgen, gewichtsverlies en een gestegen serum-thyroxineconcentratie. Uit de anamnese bleek dat de hond een “bone and raw food” dieet te eten kreeg. Dit maakte de diagnose van voedselafhankelijke hyperthyroïdie zeer waarschijnlijk. Andere mogelijke differentiaaldiagnosen werden uitgesloten door middel van een uitgebreide diagnostiek. Uiteindelijk verdwenen de symptomen en normaliseerden de schildklierwaarden na verandering naar een klassiek commercieel onderhoudsdieet. Bij elke hond met een gestegen serum-thyroxineconcentratie, met of zonder symptomen van hyperthyroïdie, is een complete voedingsanamnese noodzakelijk. Eigenaars moeten geïnformeerd worden over het feit dat diëten met rauw vlees vaak nutritionele tekortkomingen hebben, het risico van bacteriële contaminatie dragen en andere veiligheidsproblemen hebben. Daarom zouden dierenartsen dit soort voeding beter afraden.

INTRODUCTION

Canine hyperthyroidism is an uncommon endocrine disorder in contrast to feline hyperthyroidism (Nelson and Couto, 2003b). Thyroid tumors represent approximately 1.2% to 3.8% of all canine tumors and nearly 90% of the thyroid tumors are carcinomas. Thyroid carcinomas are usually large solid masses and are therefore easily palpable. Almost all dogs with thyroid neoplasia are euthyroid or hypothyroid. However, approximately 10% of these animals have functional thyroid tumors, which secrete excess thyroid hormones and therefore cause hyperthyroidism (Nelson and Couto, 2003b; Mooney, 2010; Köhler...
et al., 2012). Exogenous hyperthyroidism has rarely been reported in dogs and results from excessive intake of thyroid hormones. This can be induced by excessive administration of sodium levothyroxine or due to an impaired metabolism of levothyroxine (concurrent renal or hepatic insufficiency) in dogs treated for hypothyroidism (Feldman and Nelson, 2004). In humans, excessive consumption of meat contaminated with thyroid hormones can also lead to hyperthyroidism. Thyrotoxicosis factitia, as this disease is called in human medicine, has been reported in people eating hamburgers or excessive amounts of sausages containing thyroid tissue (Hedberg et al., 1987; Kinney et al., 1988; Parmar and Sturge, 2003; Conrey et al., 2008; Hendriks and Looij, 2010). Dietary hyperthyroidism has recently been described in dogs (Köhler et al., 2012; Zeugswetter et al., 2013).

A current trend among dog owners is the feeding of so-called "natural diets" (Joffe and Schlesinger, 2002; Köhler et al., 2012). Proponents argue that the heat used to produce commercial pet foods destroys essential nutrients and enzymes (Freeman and Michel, 2001). They also assume that the high amount of starch, especially in dry food, is inappropriate for dogs, given the low starch content of prey animals (Axelsson et al., 2013). Some argue that commercial pet foods do not meet the nutritional needs of dogs and may be a source of chronic health problems (Axelsson et al., 2013). Proponents argue that commercial pet foods do not meet the nutritional needs of dogs (Köhler et al., 2012; Zeugswetter et al., 2013).

The thought behind this dietary concept is that the wolf has evolved over many million years on a natural raw diet and therefore this would be the ideal food source for dogs (Freeman and Michel, 2001). In general, the basic material of this type of diet originates from various body parts of ruminants including neck with trachea and adherent thyroid glands. Hence, these diets may contain a large amount of raw thyroid gland tissue. Thyroid hormones are not destroyed by gastric acid and can be absorbed, similar to levothyroxine administered for the treatment of hypothyroidism (Köhler et al., 2012). This may lead to an elevated serum thyroxine concentration and clinical signs of hyperthyroidism (Köhler et al., 2012; Zeugswetter et al., 2013).

In this report, a case of dietary hyperthyroidism in a dog is described. There is particular emphasis on the differential diagnosis of an increased serum thyroxine concentration and the diagnostic steps leading to the definitive diagnosis. The case was complicated by the fact that the owners did not follow the initial advice by the authors to feed a traditional commercial maintenance diet.

**CASE REPORT**

**History and physical examination**

An eleven-month-old, male, intact Rottweiler was referred to the Department of Small Animal Medicine and Clinical Biology of the Faculty of Veterinary Medicine (UGhent) because of panting, weight loss despite a good appetite and an increased serum total thyroxine concentration (TT4) of 116 nmol/L (reference interval (RI): 13-51). According to the owners, the symptoms had suddenly occurred after a diet change, six weeks earlier. The diet of the dog had been switched from a commercial dry to a commercial BARF diet (chicken and beef, Degomeat bvba, Aalst, Belgium), and since then, the dog had lost 3 kg. There had been no change in appetite and water intake. The dog had been properly vaccinated and dewormed and had no travel history. The patient had received a treatment with corticosteroids for five days without improvement, as the referring veterinarian suspected the dog of a chronic bronchitis after taking thoracic radiographs.

At presentation, hyperactivity was observed. Body weight was 41 kg and body condition score (BCS) 4/9 (Freeman et al., 2011). The dog was panting and mildly tachycardic (136 beats per minute). The remainder of the physical examination was normal.

Based on the history and physical examination, the following problem list was made: increased TT4, weight loss despite a good appetite, intermittent panting/tachypnea, hyperactivity and mild tachycardia.

**Differential diagnosis and diagnostic approach**

The differential diagnosis for an increased TT4 is rather narrow. In this case, dietary hyperthyroidism due to feeding a BARF diet was the most likely diagnosis. A functional thyroid tumor was unlikely as the dog was very young, and there was no cervical mass palpable. Furthermore, neoplastic ectopic thyroid tissue is (extremely) rare (Mooney, 2010). Moreover, an immune mediated lymphocytic thyroiditis leading to hypothyroidism could be considered, as it is known that serum autoantibodies directed against triiodothyronine (T3) and T4 may interfere with thyroid hormone assays (Desprès and Grant, 1998; Scott-Moncrieff, 2010). These antibodies compete for hormones with antibodies used in the thyroxine assay. Depending on the separation technique used, this may lead to falsely increased or decreased thyroid hormone measurements (Desprès and Grant, 1998; Scott-Moncrieff, 2010). An increased TT4 because of exogenous thyroxine medication seemed impossible in this dog as it had not been prescribed to the dog nor to the owners. A complete history revealed that the dog had not received any medication. Finally, it has also been described that thyroid trauma (Rau et al., 2007) or prolonged storage of serum at high temperatures (Behrend et al., 1998) might cause elevations of TT4.
A complete hematology and biochemistry were performed and no significant abnormalities were observed. Radiographs of the thorax were taken as the referring veterinarian had noticed a mild broncho-interstitial pattern and to preclude other causes of the intermittent panting and tachypnea. There was a generalized but mild broncho-interstitial pattern present. Main differentials were inflammation, such as infection (parasitic or bacterial) or non-infectious inflammation (allergic, chronic bronchitis). Fibrosis and neoplasia were less likely.

The owners were informed that a dietary induced hyperthyroidism was considered very likely and that feeding a traditional commercial maintenance diet was mandatory. A control of serum TT4 concentration was advised one week later. Because of the mild generalized broncho-interstitial pattern, a fecal sample for lungworm analysis was sent to the laboratory. Meanwhile, the dog was treated with doxycyclin (10 mg/kg per oral sid, Ronaxan®, Merial) for 14 days and dewormed with fenbendazole (50 mg/kg per oral sid, Panacur®, Intervet) for five days. If no clinical and radiographic improvement would occur after the preset therapy, a bronchoscopy including broncho-alveolar lavage (BAL) was considered two weeks after cessation of the antibiotic treatment.

One week after the initial consultation, there was still a pronounced increase of serum TT4 concentration present (181 nmol/L (RI: 13-51)), and the clinical signs persisted. The fecal sample turned out to be negative for lungworms. At this time point, it was assumed that a traditional commercial diet was fed as recommended. Therefore, it seemed very unlikely that the BARF diet was the cause of the persistent increase of TT4. An immune mediated thyroiditis with a false increase of TT4 due to serum autoantibodies was considered, although the clinical symptoms were not typical. Symptoms that are commonly seen in hypothyroid dogs include lethargy, mental dullness, weight gain, unwillingness to exercise, cold intolerance, myxedema and other dermatologic changes (Scott-Moncrieff, 2010). On the other hand, it is known that clinical signs may be non-specific and insidious in onset; therefore hypothyroidism is a commonly misdiagnosed disease (Scott-Moncrieff, 2010). However, the clinical signs in this case seemed rather opposite to hypothyroidism. Further, an ectopic functional thyroid tumor was still a possibility and the expected clinical signs did include weight loss and panting. However, the rather young age of the dog and rarity of this disease made it less likely.

To preclude these causes, another week later, a scintigraphic examination of the thyroid gland was performed. A quantitative measurement of the uptake of radioactive technetium pertechnetate has a high discriminatory power in differentiating hypothyroid dogs from dogs with non-thyroidal illness (Scott-Moncrieff, 2010). Hypothyroid dogs have a median uptake of 0.16% compared to a median uptake of 0.62% in dogs with a normal thyroid function (Scott-Moncrieff, 2010). Both of the thyroid glands showed insufficient activity and were subjectively too small (Figure 1). The percentage of pertechnetate uptake was 0.02% at the left side and 0.05% at the right side, which is too low for a normal thyroid tissue. The scintigraphic findings indicated inactive thyroid tissue. This could be explained by hypothyroidism, although this was unlikely based on clinical signs. Another possible explanation was an ectopic thyroid tumor. As the episodes of tachypnea were still present, it was also considered that the dog might have two non-related medical problems. Another appointment was made one week later for a complete thyroid hormone profile and further diagnostic work-up of the respiratory symptoms.

Keeping in mind that the main clinical signs suggested hyperthyroidism rather than hypothyroidism, the owners were asked again about nutrition. Only at that point, it became clear that, despite the advice of the authors, they had changed one BARF food for another commercially available complete fresh meat diet (Duck Beef-Liver-Chicken zero gluten, Duck health food, Lennik, Belgium). Control radiographs of the thorax were taken, which still revealed...
a generalized but mild broncho-interstitial pattern. A blood sample was taken to measure free T4 (fT4) using equilibrium dialysis and was markedly increased (104 pmol/L (RI: 6-40)). Canine thyroid stimulating hormone (cTSH) was <0.03 ng/mL and thyroglobulin autoantibodies (TgAA) were negative. Circulating antithyroid hormone antibodies do not affect the fT4 results determined by the equilibrium dialysis test (Nelson and Couto, 2003a; Scott-Moncrieff, 2010). The results made hypothyroidism very unlikely and confirmed exogenous hyperthyroidism. Advice was given to stop the fresh meat diet immediately and a traditional commercial dry maintenance diet was initiated. A control visit after one month was recommended.

**Follow-up**

One month after the latest diet change, all symptoms had resolved. The dog had gained 4 kg of weight (45.3 kg) and had a BCS of 4/9. A control blood examination was performed and both fT4 (12.6 pmol/L (RI: 6-40)) and cTSH were within reference interval. The definitive diagnosis of dietary hyperthyroidism was confirmed.

Six weeks later, the owners came for a control visit, because the symptoms of intermittent panting persisted. Control radiographs of the thorax were taken again. The mild but generalized broncho-interstitial pattern was still present. Because of a suspicion of right ventricle enlargement, an echocardiography was performed, which revealed no significant abnormalities. A bronchoscopy including BAL was advised if the respiratory symptoms would persist.

Telephone contact with the owners, one year after the diagnosis of dietary hyperthyroidism, revealed that the respiratory symptoms had completely resolved.

**DISCUSSION**

Canine hyperthyroidism is a very uncommon disease. Recently, Köhler et al. (2012) reported a new case of hyperthyroxinemia in dogs, similar to dietary hyperthyroidism that has been reported in humans (Hedberg et al., 1987; Kinney et al., 1988; Parmar and Sturje, 2003; Conrey et al., 2008; Hendriks and Looj, 2010). Köhler et al. (2012) retrospectively described twelve dogs with increased plasma TT4 concentration due to the feeding of a raw meat diet. The dogs had a median age of five years and both male and female dogs were included. Dietary history revealed that eight dogs received a BARF diet and four owners fed a commercial diet with dried gullet on a daily basis (Köhler et al., 2012). Symptoms of canine hyperthyroidism include weight loss, polyphagia, polyuria/polydipsia, restlessness, aggressiveness, panting and tachycardia. These clinical signs are similar to those seen in hyperthyroid cats, although dogs tend to be less symptomatic (Mooney, 2010). Dogs with dietary hyperthyroidism may also exhibit these symptoms (Köhler et al., 2012; Zeugswetter et al., 2013). In the study of Köhler et al. (2012), weight loss was the primary complaint in most of the dogs; other clinical symptoms were restlessness, aggressiveness, tachycardia and panting. However, six dogs (50%) had no clinical signs. The median plasma TT4 concentration was 156 nmol/L (RI: 19.3-51.5), with a range of 80 to 392 nmol/L. Serum TT4 concentrations are usually very high in dogs with dietary hyperthyroidism (Köhler et al., 2012). The dog in this case also had a pronounced increase of serum TT4 and fT4 concentrations. In contrast, elevations of TT4 in dogs with hyperthyroidism due to functional thyroid neoplasia are generally moderate (Mooney, 2010). Köhler et al. (2012) measured cTSH concentrations in six dogs. Plasma cTSH was undetectable in five dogs and 0.05 ng/mL (RI: <0.3) in one dog (Köhler et al., 2012). The dog in the present case report also had an undetectable cTSH concentration. An increased serum TT4 concentration causes a negative feedback at the level of the hypothalamus and the anterior pituitary gland, resulting in an undetectably low cTSH concentration (Sjaastad et al., 2003). After changing towards a traditional commercial diet, clinical symptoms resolved and thyroid blood values normalized in all dogs of the study of Köhler et al. (2012), as was the case in the present dog.

Zeugswetter et al. (2013) described the same phenomenon in two female, spayed dogs. The dogs belonged to the same owner and were referred for further examination because of clinical signs (polyuria, polydipsia, restlessness, tachycardia and excessive panting) and laboratory values compatible with hyperthyroidism. For both of the dogs the TT4 concentration was 193 nmol/L (RI: 17-58) and cTSH was 0.03 ng/mL (RI: <0.6). Ultrasound examination of the ventral aspect of the neck showed small thyroid glands in both dogs, because of the chronic negative feedback. Dietary history revealed that the dogs were fed meat containing thyroid gland tissue (Zeugswetter et al., 2013).

The dog in this case had a history of receiving a commercial BARF diet, a distinct increase in serum TT4 concentration and also clinical signs, which suited perfectly with hyperthyroidism. Assuming that the BARF diet was stopped, the authors were misled when clinical symptoms persisted and the serum TT4 concentration remained increased. At that time point, immune mediated thyroiditis was also a possible differential diagnosis, although the symptoms were difficult to explain by hypothyroidism. An increase in serum TT4 because of autoantibodies directed against T4 has been described. These antibodies have been detected in less than 2% of the samples from dogs with suspected hypothyroidism (Scott-Moncrieff, 2010). The scintigraphic examination of the present dog showed inactive thyroid tissue. However, dietary thyrotoxicosis itself may also cause atrophy of
In conclusion, raw food diets are regarded as major nutritional risk factor. If the feeding of a non-conventional diet is mentioned in the anamnesis, a detailed nutritional screening is necessary (Freeman et al., 2011).

CONCLUSION

Dietary hyperthyroidism can occur in dogs fed raw food diets. The work-up of every dog with an increased serum TT₄ concentration, with or without clinical signs of hyperthyroidism, should include a thorough dietary history. Owners should be informed and veterinarians should recommend against feeding these diets.

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