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Dietary hyperthyroidism in a Rottweiler

Voedselgerelateerde hyperthyroïdie bij een rottweiler

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A BSTRACT

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 onderhoudsdiëet. 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 (Joffe and Schlesinger, 2002). A well-known "natural diet" is the bone and raw food (BARF) diet (Freeman and Michel, 2001; Joffe and Schlesinger, 2002; Köhler et al., 2012). This diet consists of 60% raw, meaty bones and is supplemented with a wide variety of ingredients, such as green vegetables (to mimic stomach contents of prey), offal (liver, kidneys, etc.), eggs, milk, yoghurt and small amounts of grains and legumes. 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 (Després 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 (Després 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.

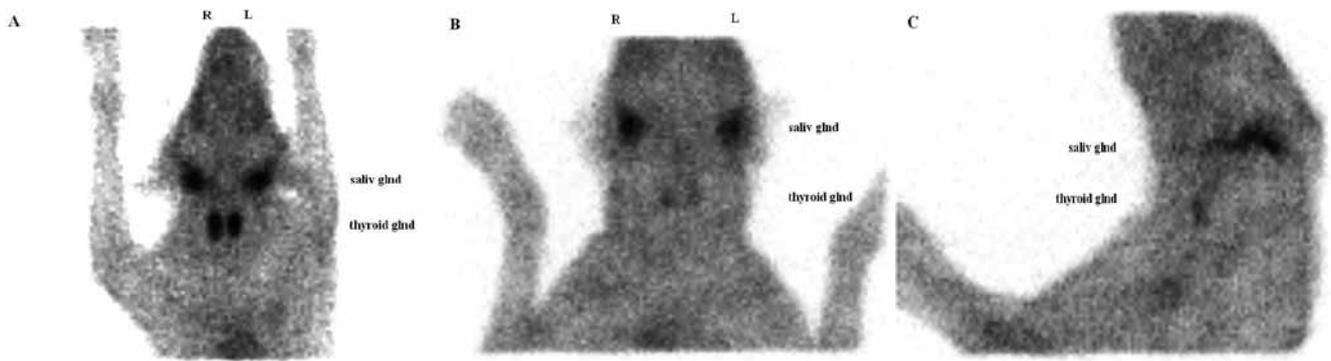


Figure 1. Scintigraphic ventral image of the thyroid gland of a normal dog (A) compared to a ventral (B) and left lateral (C) image of the dog diagnosed with dietary hyperthyroidism. Saliv gland: salivary gland; thyroid gland: thyroid gland; L: left; R: right.

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 TT_4 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 TT_4 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 TT_4 . An immune mediated thyroiditis with a false increase of TT_4 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 in-

sidious 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 function. There was no ectopic thyroid tissue visible. 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 a suppression of the thyroid function due to exogenous thyroid hormones. 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 cause of hyperthyroxinemia in dogs, similar to dietary hyperthyroidism that has been reported in humans (Hedberg et al., 1987; Kinney et al., 1988; Parmar and Sturge, 2003; Conrey et al., 2008; Hendriks and Looij, 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

the thyroid gland, because of the negative feedback at the level of the hypothalamus and the anterior pituitary gland (Sjaastad et al., 2003). It was only after reevaluating the case and the change towards a traditional commercial maintenance diet, that the definitive diagnosis of dietary hyperthyroidism was made.

Nowadays, veterinarians must deal with pet owners who have wide access to information and misinformation on small animal nutrition. There is an enormous amount of diets available and consequently, there are also a growing number of unconventional diets being promoted for dogs and cats. It is easy to understand why owners have such a strong appeal to nutrition. Most pet owners approach their animals as family members. Food has a social significance and giving food is conceived as a way of showing affection. Diet is also something that an owner can easily control (Freeman and Michel, 2001; Michel 2006; Schlesinger and Joffe, 2011).

In recent years, many pet owners have a growing interest in 'natural' and homemade diets, instead of conventional commercial choices, such as extruded and canned diets. This has been partially driven by a movement paralleled in the human food marketplace for natural and organic products (Schlesinger and Joffe, 2011). A recent study in Germany revealed that approximately 8% of the dog owners and <1% of the cat owners feed their pets with homemade diets (Becker et al., 2012). One of the most well-known unconventional diets is the raw food diets (Freeman and Michel, 2001). Motivations of dog or cat owners to change the feeding to these type of diets are diverse (Michel, 2006). Proponents claim numerous benefits, such as improvement in coat and skin, elimination of breath, body and feces odor, improvement in amount of energy and behavior and improvement in overall health and immune function (Freeman and Michel, 2001). However, these arguments are not supported by scientific evidence, and all the alleged health benefits are anecdotal. Actually, there are numerous disadvantages of feeding raw food diets. First, these diets tend to be nutritionally imbalanced. Nearly all of these diets have been found to have nutrient excesses or deficiencies that may cause serious health problems on a long-term basis (Freeman and Michel, 2001; Michel, 2006; Dillitzer et al., 2011). Dillitzer et al. (2011) evaluated the vitamin and mineral content of 95 BARF rations. Not less than 60% of these diets were nutritionally imbalanced or had a seriously unbalanced Ca:P ratio (Dillitzer et al., 2011). Especially young, growing animals are at risk for inappropriate dietary vitamin and mineral contents (Michel, 2006). Nutritional secondary hyperparathyroidism has been reported in a litter of German shepherd puppies fed a diet consisting of 80% steamed rice and 20% raw meat. The diet contained too much phosphorus and the puppies showed limb deformation (Kawaguchi et al., 1993). Delay and Laing (2002) reported nutritional osteodystrophy in two litters of large breed puppies fed a BARF diet from about three weeks of

age (Delay and Laing, 2002).

Secondly, uncooked products carry the risk of bacterial contamination (Freeman and Michel, 2001; Michel, 2006). Joffe and Schlesinger (2002) found that 80% of the homeprepared BARF diets containing chicken were contaminated with *Salmonella* species. Other similar investigations found evidence of *Escherichia coli*, *Toxoplasma gondii* and *Cryptosporidium* species (Lucas et al., 1999; Weese et al., 2005; Strohmeyer et al., 2006). There have been no reports published about clinical salmonellosis in dogs fed a BARF diet, although *Salmonella* species are well-described pathogens in dogs (Joffe and Schlesinger, 2002). Proponents argue that dogs are more resistant against bacteria than people, but so far, this has not been proven (Freeman and Michel, 2001). Moreover, owners are also at risk because they may come in contact with contaminated food through the preparation and feeding of a raw diet (Michel, 2006). People should also be aware of the fact that dogs fed raw food diets, potentially shed bacteria in their stools, which can be a source of infection (Schlesinger and Joffe, 2011). Especially young, elderly or immunocompromised people must be careful (Freeman and Michel, 2001). Thus, feeding raw food diets not only concerns individual pets, it has become a community health issue (AHAA, 2011).

Finally, there are other potential problems with raw food diets regarding safety. The raw bones included in many BARF diets may result in intestinal obstruction, gastrointestinal perforation, gastroenteritis and fractured teeth (Freeman and Michel, 2001; Michel, 2006).

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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