Case Report Rapport de cas

Thyrotoxicosis in a dog induced by the consumption of feces from a levothyroxine-supplemented housemate

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Abstract — A 9-year-old golden retriever dog was evaluated for polyuria, polydipsia, weight loss, and elevated serum thyroxine. Targeted questioning revealed that the dog was coprophagic and routinely ingested the feces of a dog that was treated with twice-daily levothyroxine. Clinical signs resolved and serum thyroxine decreased to normal levels in the affected dog with prevention of coprophagy.

Résumé — Thyrotoxicose chez un chien induite par la consommation de fèces d'un compagnon prenant des suppléments de lévothyroxine. Un chien Golden retriever âgé de 9 ans a été évalué pour la polyurie, la polydipsie, la perte de poids et la thyroxine sérique élevée. Des questions ciblées ont révélé que le chien était coprophage et ingérait régulièrement les fèces d'un chien qui était traité deux fois par jour à la lévothyroxine. Les signes cliniques se sont résorbés et la thyroxine sérique a baissé à des niveaux normaux chez le chien affecté avec la prévention de la coprophagie.

(Traduit par Isabelle Vallières)

Can Vet J 2013;54:987–989

Hyperthyroidism is rare in dogs and is generally associated with a functional thyroid adenocarcinoma. Although cases of thyrotoxicosis have been reported in dogs receiving thyroxine supplementation for treatment of hypothyroidism, reports of the deleterious effects on untreated contact animals are lacking. This report describes the presentation, diagnostic evaluation, treatment, and resolution of clinical signs in a dog with thyrotoxicosis secondary to ingestion of feces from a canine housemate treated with levothyroxine. This paper should raise awareness of the potential risks associated with treatment for hypothyroidism and describes a new exogenous cause for canine hyperthyroidism.

Case description

A 9-year-old spayed female golden retriever dog was referred to the Oncology Service at the University of Illinois Veterinary Teaching Hospital for suspected ectopic thyroid carcinoma. The dog had been taken to the referring veterinarian with a 2-month history of polyphagia, polydipsia, polyuria, and weight loss of approximately 9 kg. Initial testing showed an increased serum thyroxine (T_4) concentration [71.0 nmol/L; reference interval (RI): 12.9 to 51.6 nmol/L] (VetScan Whole Blood Analyzer; Abaxis North America, Union City, California, USA) (1). Repeat testing 2 wk later showed that total T_4 was unchanged and there was an increased serum free-T_4 concentration (57 pmol/L; RI: 8 to 40 pmol/L) by equilibrium dialysis (Antech Diagnostics, Irvine, California, USA). Based upon a preliminary diagnosis of hyperthyroidism, the referring veterinarian performed a cervical surgical exploratory examination, during which no thyroid tissue (normal or abnormal) was identified. The hyperthyroidism was then presumed to be related to ectopic thyroid tissue and the dog was referred for further management.

On presentation, the dog was bright and alert, weighing 28.2 kg with a body condition score of 4/9. Physical examination showed a healing ventral cervical incision around which the fur was shaved from the cervical exploratory surgery performed 3 d prior to presentation, moderate bilateral ceruminous otic debris, and tear staining under both eyes. Tachycardia of 140 beats/min and panting were also noted at rest. The remainder of the evaluation, including a complete neurological examination, was considered normal. On initial laboratory evaluation, the only hematological abnormality was a moderate eosinophilia (2120/μL; RI: 100 to 1000/μL). Biochemical abnormalities included a mild hypoglobulinemia (25 g/L; RI: 27 to 44 g/L), a mild increase in serum alanine aminotransferase (ALT) activity (122 U/L; RI: 17 to 87 U/L), a decreased serum gamma-glutamyl transferase (GGT) activity (0 U/L; RI: 1 to 11 U/L), and a decreased serum bicarbonate concentration (16.1 mmol/L; RI: 17.0 to 29.0 mmol/L). T4 was not measured at this time. Urinalysis showed a urine specific gravity of 1.018 and urine pH

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of 8.0. Abdominal ultrasonography was unremarkable. Cervical ultrasonography identified normal thyroid gland tissue.

A functional ectopic thyroid adenocarcinoma was suspected based on the presence of hyperthyroidism without an associated thyroid mass. To evaluate for ectopic thyroid tissue, nuclear scintigraphy of the head and thorax was performed under sedation utilizing IV 4.7 mCi 99m-Tc-O4. There was minimal to no uptake of the technetium radiopharmaceutical by the thyroid gland, normal uptake in the salivary glands and uptake in gastric contents (resulting from swallowed salivary secretions). These results were consistent with iatrogenic hyperthyroidism secondary to the administration of exogenous thyroid hormone. The dog remained hospitalized overnight for clearance of the radiopharmaceutical and return to background radioactivity levels.

When queried about possible sources of exogenous thyroxine, the owner related that another household dog was currently receiving 0.8 mg levothyroxine q12h for hypothyroidism. The owner was certain that he had not been medicating the wrong animal, the medication was kept out of reach of both animals, and there was no possibility of accidental ingestion of the levothyroxine by this patient. Once the patient was released from radiation quarantine her serum T_4 and serum thyroid stimulating hormone (TSH) concentrations were reassessed since there was no possibility of exogenous thyroxine exposure while hospitalized. Results showed that total T_4 had returned to normal (19.0 nmol/L; RI: 15.0 to 48.0 nmol/L) and the TSH concentration was undetectable (< 0.03 ng/mL; RI: 0.0 to 1.0 ng/mL). The owner was advised that exogenous thyroid hormone was the likely cause of the patient's presenting clinical signs; this was again dismissed by the owner as impossible. Subsequently, the owner requested further investigation of the cause of the transient hyperthyroidism. The possibility of functional ectopic thyroid tissue in the abdomen, reported in humans but not in dogs, was discussed but considered unlikely (2). The owner pressed for additional testing and a second technetium scan encompassing the head, thorax, and abdomen was performed using IV 4.85 mCi of 99m-Tc-O_4. The results were consistent with the original scan with minimal to no uptake by the thyroid glands, and apart from visible radiopharmaceutical in the gastric secretions, no appreciable uptake by any tissue in the abdomen. The patient was again quarantined overnight for clearance of the radiopharmaceutical. A second total T_4/TSH panel was submitted the following day. The total T_4 was now significantly subnormal (< 6.44 nmol/L; RI: 15.0 to 48.0 nmol/L) and the TSH had increased to within the normal range (0.048 ng/mL; RI: 0.0 to 1.0 ng/mL).

A diagnosis of thyrotoxicosis secondary to exogenous thyroid hormone administration was made, though how the hormone was supplemented was still unclear. During discharge counseling, the owner continued to refute the diagnosis until he admitted that the patient routinely ingested the feces from the medicated housemate. The treatment recommendations were subsequently updated to include aggressive cleaning of the yard to prevent any continued coprophagia.

After discharge, the patient developed diarrhea that lasted 4 d but resolved by day 7. By day 12 after discharge, the owner reported complete resolution of the dog's clinical signs with no intervention other than routine removal of feces from the back yard. A serum T_4 concentration approximately 4 mo after discharge was within normal limits (16.8 nmol/L; RI: 12.9 to 51.6 nmol/L). A subsequent request for a sample of the housemate dog's feces was declined because the housemate had died of unrelated causes. The case history, nuclear scintigraphy findings, and progression of changes in T4 and TSH levels before and after control of coprophagy support a diagnosis of secondary hyperthyroidism in this dog from ingestion of feces from another animal supplemented with thyroid hormone.

Discussion

Thyroid disease in dogs is usually associated with hypothyroidism rather than excessive T_4 production. Hyperthyroidism in dogs is typically associated with a functional thyroid adenocarcinoma, although functional adenomas have been reported (3,4). The risk for thyroid tumors increases with age and breed predispositions have been reported; the golden retriever is one breed consistently noted to be over-represented (3). Overall, thyroid neoplasia accounts for approximately 1% to 2% of all reported canine neoplastic diseases (3).

Dogs with confirmed thyroid neoplasia generally present because of a visible or palpable cervical mass or associated signs of dysphagia, cough, and dysphonia (3). Rarely, dogs may present with diffuse swelling of the neck from venous or lymphatic occlusion or cardiovascular collapse due to erosion of major blood vessels (5,6). Affected dogs are usually not clinically hyperthyroid and thyroid hormone concentrations are typically normal. In one study, no dogs with thyroid neoplasia had elevated thyroid hormone concentrations (7). In another study, T4 elevations were present in 31% of 65 affected dogs, but only 2 (3%) showed clinical signs consistent with thyrotoxicosis (8). The dog herein had multiple clinical signs of thyrotoxicosis, including polyuria, polydipsia, polyphagia, weight loss, and resting tachycardia (9,10).

In addition to the increased T_4 concentration, multiple clinicopathologic abnormalities were noted in this patient. Mildly increased serum ALT activity was attributed to the dog's hyperthyroidism. Increased ALT activity is a common finding in cats with hyperthyroidism and it is reasonable to expect this finding in similarly affected canine patients (11). Other laboratory abnormalities did not appear to be linked to thyrotoxicosis. The moderate eosinophilia could be related to continued intestinal parasite exposure with chronic coprophagia. Alternatively, mild eosinophilia has been reported in a small number of hyperthyroid cats and may be secondary to a relative decrease in available cortisol due to excessive circulating thyroid hormone, but this possibility was not tested by re-evaluation of this parameter after resolution of this dog's hyperthyroidism (11). The mild hypoglobulinemia may reflect a relatively low level of antigenic stimulation, immune suppression, or, more likely, a normal value for this patient. Likewise, the undetectable GGT activity was not clinically important and likely represented a value normal for this specific patient. Lastly, the mild decrease in bicarbonate may have represented a mild metabolic acidosis that was compensating for a respiratory alkalosis due to chronic panting (12).

The results of this diagnostic work-up, including serial decreases in thyroxine levels and a rise in TSH without home exposure strongly suggest this dog's hyperthyroidism was iatrogenic. Due to the persistent clinical signs and documented increases in T_4 over at least 2 wk, it is unlikely accidental ingestion of the medication was a cause for the thyrotoxicosis. Because early questioning of the owner about the potential for exposure to thyroid hormone supplementation was emphatically refuted, a more thorough investigation into the cause for the dog's hyperthyroid status was pursued. The presence of increased circulating T_4 without technetium uptake by any tissue other than the salivary glands is nearly pathognomonic for an exogenous source (13). Uptake of technetium within the stomach could have obscured the presence of functional ectopic thyroid tissue within the gastric wall; however, resolution of clinical signs with the recommended treatment (i.e., removal of feces) would not have occurred. Support for iatrogenic disease was also investigated by using hospitalization to prevent further supplementation. The results of blood analysis over the course of 4 d showed the expected decrease in circulating T_4 with concurrent resolution of suppression of TSH.

Thyroid hormone pharmacokinetics are highly variable in the dog with as much as 40% of an administered dose of levothyroxine excreted in the feces (14). Circulating T_4 is also eliminated in the feces (15). Bioavailability of commercial thyroid hormone replacement drugs is dependent on drug formulation, recent ingestion of food, diet, and considerable individual patient variability (16,17). High fecal concentrations of T_4 might be explained if the housemate was routinely fed prior to medicating, had a diet low in fatty acids, or had abnormally poor intestinal absorption (16,17). It has been suggested that dogs are relatively resistant to thyrotoxicosis with doses upwards of 10 to 20 times the therapeutic dose required to induce clinical signs (18). Although this may be generally true, reports exist of dogs exhibiting signs of thyrotoxicosis with much lower doses (10). A recent publication describes the development of thyrotoxicosis in 6 dogs that were on a raw diet (19). Although the thyroid hormone content of this diet was not determined, it is another example of thyrotoxicosis due to chronic, unintentional ingestion of thyroid hormone. In the case presented here, evaluation of the thyroid hormone content of the housemate's feces was precluded when that dog died prior to finding a suitable method for fecal T_4 determination. A recent study evaluating the measurement of thyroid status of multiple species of wildlife using fecal samples has been published and would have proven useful if a fecal sample could have been collected (15). Nonetheless, this would not have fully characterized the dose ingested by the case dog without an accurate measure of the fecal volume ingested, a value which could not be determined without allowing the case dog to continue the coprophagy which precipitated the clinical problem.

To the authors' knowledge, this is the first reported case of iatrogenic hyperthyroidism due to coprophagia in the dog. Although potentially a rare occurrence, it highlights the need to obtain a careful and comprehensive history in cases in which an iatrogenic etiology cannot be substantiated. This case suggests adding questions regarding peculiarities about the patient's unusual habits as well as the presence and health status of other animals in the household. With a large number of dogs receiving supplementation for hypothyroidism, there is a significant potential for toxic exposures to thyroid hormone medications. Indirect exposure (i.e., coprophagia) should also be considered in these cases. CVJ

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