Dilated Cardiomyopathy in a Fila Brasileiro with Hypothyroidism Secondary to Lymphocytic Thyroiditis

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ABSTRACT

Background: Hypothyroidism is a common disease in middle-aged purebred dogs and is characterized by reduced plasma concentrations of thyroid hormones. These hormones have important modulatory effects on myocardial chronotropism and inotropism, and when heart disease is linked to hypothyroidism, disease progression may be accelerated. Dilated cardiomyopathy (DCM) often occurs in association with hypothyroidism. However, an etiologic contribution of lower thyroid hormone concentrations towards the development and progression of DCM is still unclear. The aim of this study was to describe a case of DCM in a Fila Brasileiro dog with hypothyroidism secondary to lymphocytic thyroiditis.

Case: A male, 11-year-old Fila Brasileiro dog was referred to the Division of Endocrinology and Metabolism of the Veterinary Clinical Hospital of the Universidade Federal do Rio Grande do Sul due to keratoconjunctivitis sicca, weight gain, apathy, and hyporexia. A primary diagnosis of hypothyroidism was made based on clinical features of hypothermia (37.8°C), bradycardia (78 bpm) with bradysphygmia, facial myxedema, bilaterally symmetrical alopecia, and hyperpigmentation of the skin with tail involvement associated with normocytic hypochromic anemia (RBC 4.76 x10⁶/mm³, Ht = 29% and Hb = 9.2 g/dL), reduced concentration of biphasic free T4 (0.22 ng/mL - reference value 0.62 - 3.11 ng/mL) and high level of cTSH (0.81 ng/mL - reference values 0.05 - 0.5 ng/mL), despite total cholesterol concentration within reference values (242 mg/dL). Oral therapy with synthetic levothyroxine (5 µg/kg) was initiated and weekly adjusted until a total daily dose of 22 µg/kg was reached. After three weeks, the patient was found dead by his owners after feeling extremely apathetic, anorexic, and adipsic the day before. At necropsy, there were congestive heart failure features such as ascites associated with liver and pulmonary congestion and an enlarged and globose heart with bilateral ventricular dilatation and whitish areas in the myocardium. Both thyroids were pale and small. Histopathological examination of the heart and thyroid showed adipocyte infiltration associated with fatty degeneration in the myocardium and marked lymphocytic-plasmacytic thyroiditis, respectively.

Discussion: All of the clinical and laboratory features presented by this dog were in complete agreement with the clinical and pathological features of canine hypothyroidism, except for total cholesterol concentrations within reference values. Although hypothyroidism is recognized as a metabolic dysfunction that may worsen a preexisting heart disease and is often associated with DCM, some studies fail to show a relationship between these diseases. The fact that the majority of giant dogs that develop DCM actually have a form of disease associated with atrophy and decreased concentration of myofibrils is straightforward, with a possible link between hypothyroidism and the etiology and/or progression of DCM in this case, once fatty degeneration of muscles is a common feature of chronically reduced thyroid hormones concentration exposure. It might also be observed that primary hypothyroidism was undoubtedly confirmed by the hormone panel blood tests and histopathological analysis. Therefore, the present report provides evidence of and is in agreement with the possible role of hypothyroidism in the pathogenesis and progression of DCM in dogs. Moreover, attention should be paid during initial thyroxine supplementation in senior dogs with hypothyroidism, thereby allowing for the early identification of any other occult disease and occasional adverse effects of medication associated with poor outcomes.

Keywords: heart disease, thyroid hormone therapy, autoimmunity, dogs.
INTRODUCTION

Hypothyroidism, diagnosed mainly among middle-aged purebred dogs, is a multisystemic endocrine disorder, characterized by the lower concentration of circulating thyroxine (T₄) and triiodothyronine (T₃) [13]. These thyroid hormones (THs) stimulate diverse metabolic activities in different systems, exerting positive inotropic and chronotropic effects on the cardiovascular system. At low concentrations, THs prompt the development of metabolic, dermatological, and neuromuscular clinical signs, in addition to cardiovascular disorders, being occasionally associated with dilated cardiomyopathy (DCM) [18]. However, a possible influence of low THs concentrations on the etiology and progression of DCM is still controversial [2,8].

Lymphocytic thyroiditis is the major cause of hypothyroidism in dogs and is present in more than 50% of these patients, causing immunomediated destruction of the thyroid gland due to diffuse infiltration of macrophages, plasma cells, and lymphocytes into the glandular parenchyma [7,20].

The aim of the present case report is to describe the main clinical and histopathological findings of a Fila dog with DCM associated with hypothyroidism secondary to lymphocytic thyroiditis.

CASE

A male, 11-year-old Fila Brasileiro dog was referred to the Division of Endocrinology and Metabolism of the Veterinary Clinical Hospital of the Universidade Federal do Rio Grande do Sul (HCV-UFRGS). The patient had a previous history of keratoconjunctivitis sicca for 13 months, weight gain (from 59 kg to 70 kg), apathy, and hyporexia. The owner reported that the dog was prostrated and that he would be lying down most of the time, without interacting with other dogs.

The physical examination showed rectal temperature of 37.8°C, bradycardia (78 bpm), and bradysphygmia, with no abnormal rhythm or murmur. The patient did not have enlarged lymph nodes and was properly hydrated. The skin examination revealed facial myxedema and bilaterally symmetrical ventrolateral hair thinning (Figure 1A) associated with alopecia and hyperpigmentation of the tail (Figure 1B).

Additional tests indicated hypoalbuminemia, i.e., albumin level of 22 g/L (reference values = 26 - 33 g/L), and normocytic hypochromic anemia (RBC = 4.76 x10⁶/mm³, Ht = 29% and Hb = 9.2 g/dL). The total cholesterol level was equal to 242 mg/dL, i.e., it fell within the normal range (150 - 270 mg/dL). The presumptive diagnosis of hypothyroidism was made based on the patient’s clinical picture, and a hormone panel blood test was requested. The low level of biphasic free T4 (0.22 ng/mL, reference values: 0.62 to 3.11 ng/mL) and high level of canine thyroid-stimulating hormone (cTSH) (0.81 ng/mL, reference value: 0.05
to 0.5 ng/mL) confirmed the presence of primary hypothyroidism.

The treatment consisted of oral levothyroxine sodium (Synthroid)\(^1\), at a total dose of 22 mcg/kg. However, levothyroxine sodium therapy started with a dose of 5 mcg/kg until the total dose was reached, being readjusted to another 5 mcg/kg every seven days up to the total dose. After nearly three weeks of treatment, while the levothyroxine dose was being gradually increased, the patient was found dead by his owners, in the morning, after having severe apathy, adipsia, and anorexia the day before.

At necropsy, besides skin lesions, there were marked ascites, severe liver congestion, with a lobular pattern (nutmeg liver), edema, pulmonary congestion, and a pale, globose, enlarged heart as a result of pronounced dilatation of both ventricles (Figure 2A and 2B). The thyroid glands were small and pale (Figure 2C). The histological examination showed multifocal and pronounced adipose infiltration in cardiomyocytes. There were sharp reduction of thyroid acini, diffuse and pronounced infiltrate of lymphocytes, and to a lesser extent, of macrophages, in addition to mild proliferation of connective tissue, indicating lymphocytic thyroiditis (Figure 2D).

**Figure 2.** Dilated cardiomyopathy in a dog with hypothyroidism. A. Globose and enlarged heart. B. Pronounced bilateral ventricular dilatation. C. Extremely small and pale thyroid gland. D. Thyroid. Intense lymphocyte infiltrate (thin arrows) with occasional plasma cells (thick arrows). Rare thyroid follicles (asterisk) in addition to mild proliferation (x) of connective tissue (HE, 400x).

**DISCUSSION**

Thyroid hormones have positive chronotropic and inotropic effects on the heart, in addition to catabolic effects on the muscle and adipose tissues, stimulating erythropoiesis and regulating the synthesis and degradation of cholesterol, thereby explaining cardiac, metabolic, and hematological consequences in the presence of low THs concentrations [8]. The homeostasis of THs maintains the contractility and functionality of the heart within physiological patterns [4], also influencing the capacity of cardiac contraction and relaxation, thus regulating the diastolic and systolic functions of the myocardium [5]. Therefore, a preexisting cardiomyopathy is expected to worsen after the development of hypothyroidism in dogs [6,8]. Nonetheless, although it is known that hypothyroidism may play a role in the development and progression of DCM, studies have failed to demonstrate a relationship between these two diseases [2].

The significant cardiovascular findings observed in animals with hypothyroidism include bradycardia and low QRS wave amplitude on the electrocardiogram [17]. A study showed that dogs with hypothyroidism have prolonged atrioventricular conduction time and ventricular action potential dura-
tion [21]. The reduction in the final diameter of the left ventricle in diastole is also an important finding in dogs with hypothyroidism [16]. Other authors also report that hypothyroidism compromises left ventricular function, exacerbating myocardial dysfunction, which may lead to heart failure and DCM [9,12].

The diagnosis of DCM in the dog in this report was based on gross and microscopic findings. This is a disease that is commonly diagnosed among large-sized and giant dogs [14,22]. In the present report, adipocyte infiltration in cardiomyocytes was the major histopathological finding. Nevertheless, the most common type of DCM in large-sized and giant dogs is histologically associated with atrophy or decreased concentration of myofibrils without adipocyte infiltration [23]. The fact that the histological profile of DCM in this case was associated with adipocyte infiltration might be related to the possible role of hypothyroidism in the pathogenesis of DCM, as this histological finding is often observed in the heart of dogs with hypothyroidism [7,19].

Lymphocytic thyroiditis is the main cause of hypothyroidism in dogs, and the morphological pattern shown by the histopathological examination clearly indicates this etiology [7,20]. Skin disorders occur in approximately 60-80% of dogs with hypothyroidism, characterized especially by tail alopecia, myxedema, and bilaterally symmetrical hypotrichosis patterns unrelated to inflammatory markers, as observed in the present report [6]. Weight gain is also a characteristic of the disease and has been documented in over 50% of patients with hypothyroidism, being one of the major complaints made by dog owners [15]. In the present report, the dog put on 11 kg in less than three months, and that was one of the reasons that led the owner to seek veterinary care for her dog. Curiously enough, the decrease in metabolic rate associated with hypothyroidism, leading to weight gain, compensated for the decrease in metabolic rate associated with hypothyroidism. However, intolerance to exercise, fatigue, and apathy may be attributed both to hypothyroidism and to DCM. In hypothyroidism, these signs may be present due to nerve conduction deficits [7], which could also explain the presence of keratoconjunctivitis sicca, a frequent finding in dogs with hypothyroidism [18]. In addition, possible causes for keratoconjunctivitis sicca are the high levels of cholesterol and triglycerides, which may predispose to the development of corneal dystrophy [10]; however, in the present report, the patient did not show associated dyslipidemia. The absence of hypercholesterolemia and the mild hypalbuminemia may have resulted from severe hyporexia associated with a nutritionally poor commercial diet. The lack of direct stimulatory effect of THs on bone marrow erythroid precursors and the decrease in peripheral oxygen demand appear to be accountable for the non-regenerative normocytic hypochromic anemia shown by the patient, which is commonly found in animals with hypothyroidism [1,24].

Finally, in this case, as a result of severe DCM, the patient apparently did not tolerate the positive inotropic and chronotropic effect caused by the initial hormone therapy, which eventually led to his sudden death. This finding underscores the necessity for slow and gradual introduction of levothyroxine in patients with hypothyroidism, especially in senior dogs or in those in which there might be occult diseases that could be exacerbated after THs replacement therapy. In conclusion, this report on two diseases commonly observed in clinical practice provides evidence that hypothyroidism may have had a crucial role in the etiology and progression of DCM.

REFERENCES