

Canine Hypothyroidism with Neurological Disorders

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ABSTRACT

Background: Hypothyroidism is characterized by hypofunction of the thyroid gland. It results in deficient production of thyroid hormones. Neurological disorders resulting from hypothyroidism are rare, which highlights the importance of this study. This study reports a case of hypothyroidism in a dog with neurological clinical signs, that was treated at the Universidade Estadual de Santa Cruz's Veterinary Hospital (HV-UESC).

Case: A 4-year-old male intact Dogo Argentino breed dog, weighing 64 kg, presenting obesity, anorexia, prostration, walking in circles, and chronic dermatopathy was presented at HV-UESC. Upon physical examination, the animal presented a deficit of proprioception in the 4 limbs, with preserved superficial and deep pain. No alteration was observed in the ears, that could explained the clinical signs. In terms of dermatopathy, the animal presented symmetrical alopecia in the lateral region of the thighs and tail. Blood samples were collected for a complete blood count and biochemical tests of urea, creatinine, ALT, AST and cholesterol. Imaging radiography and ultrasonography were performed, which ruled out thoracic and abdominal changes that could be related to the case. Prior to receiving the blood test results, idiopathic encephalitis was suspected and enrofloxacin and prednisone were prescribed for 7 days. During the medication period, previous exams were provided, which indicated only increased cholesterol (500 mg/dL). The animal showed no improvement with the prescribed medication. In view of the clinical signs presented by the patient and the results of the additional tests, hormonal disease was suspected, compatible with hypothyroidism. Thus, hormonal tests of total T4, free T4, and TSH were requested, leading to verification of reduced total T4 (0.3 ng/dL) and free T4 (0.15 ng/dL) levels, and confirming the dysfunction of the thyroid gland. The previous treatment was suspended and thyroid hormone replacement was initiated. After 3 days of treatment, the neurological signs regressed and the animal became more active; after 30 days, the areas of alopecia decreased. Although the patient did not receive the recommended clinical follow-up for such cases, it was possible to establish the ideal levothyroxine dosage for the dog after appropriate adjustments, which permitted thyroid hormone levels to return to normal.

Discussion: This report refers to a case of hypothyroidism in a giant dog breed. The dog in the report showed clinical signs of a dermatological, metabolic, and neurological nature, which is consistent with a lack of thyroid hormone. The main signs presented by the animal were neurological, such as walking in circles and a deficit of proprioception in the four limbs. These clinical signs are rarely mentioned in the literature associated with hypothyroidism. Laboratory abnormalities are correlated with the severity and chronicity of the disease. The animal showed a decrease in total T4 and free T4, which is to be expected in a hypothyroid animal. As a result, levothyroxine replacement treatment was initiated. The dose used for the dog, which is the recommended dose in the literature, greatly increased its total T4 levels. As a result, the dose was readjusted after a new clinical evaluation. The rate of metabolism and absorption of levothyroxine varies widely and is independent of weight. The patient showed quickly improvement in neurological signs, activity level, and serum cholesterol rate. Regarding dermatological signs and body condition, there was a more gradual improvement. This corroborates what is mentioned in the literature, which indicates that improvements can take many months.

Keywords: hormonal Disease, hypothyroidism, neuropathy.

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INTRODUCTION

Hypothyroidism is a common endocrine disease in dogs. It is the result of a deficiency of the active thyroid hormones triiodothyronine (T3) and thyroxine (T4) [14]. Defects at any level of the hypothalamic-pituitary-thyroid axis can lead to deficient secretion of these hormones. Hypothyroidism can be classified as primary or central, and both forms can be congenital or acquired. The central condition is rare compared to primary hypothyroidism [1].

Clinical signs of hypothyroidism are generally nonspecific and no single sign or classical combination of signs is absolutely consistent with the disorder. Being overweight and lethargic are characteristics that are commonly observed in dogs with hypothyroidism [9]. Neurological signs associated with hypothyroidism are rare. When they do occur, the most frequently described are head tilt, ataxia, walking in circles, and strabismus [18].

Diagnosis of hypothyroidism depends largely on evaluation of the thyroid, through hormonal dosages (total T4 and free T4), and endogenous canine thyroid stimulating hormone (TSH) [14].

Treatment of this endocrine disease is based on lifetime oral replacement with a synthetic thyroid hormone, which must be accompanied by a veterinarian [10].

Thus, considering that hypothyroidism is a common condition in routine veterinary clinical care of dogs and can affect the quality of life of affected animals, the aim of this report was to describe a case of hypothyroidism in a dog with neurological clinical signs that are rarely described in the literature.

CASE

A 4-year-old male intact Dogo Argentino breed dog, weighing 64 kg, presenting obesity, anorexia, prostration, walking in circles (Figure 1), and chronic dermatopathy was treated at the Universidade Estadual de Santa Cruz's (UESC) Veterinary Hospital. The trainer reported that the animal was prostrate, spent all day lying down, and did not get up even to feed.

A physical examination showed that the animal presented a proprioception deficit in all 4 limbs, but with preserved superficial and deep pain, and walked in circles compulsively. Examination of the cranial nerves showed no alterations. In terms of dermatopathy, the animal presented symmetrical alopecia in the lateral

region of the thighs and tail. It had previously been diagnosed with generalized demodicosis while still a puppy and with pyoderma after reaching adulthood. Frequent use of topical chlorhexidine-based products was reported.

Blood was taken from the animal for a blood count and measurement of urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and cholesterol. Imaging tests (radiography and ultrasonography) were also performed, which ruled out the suspicion of neoplasia or other alteration that could have explained the clinical signs. During the consultation, idiopathic encephalitis was suspected and Enrofloxacin¹ [Baytril[®] - 5 mg/kg, p.o., QD, for 7 days] and Prednisone² [Prediderm[®] - 1 mg/kg, p.o., QD, for 7 days] were prescribed.

Three days after blood collection, the animal did not show any improvement with the prescribed medication, but the results of the requested tests were received. The blood count results showed that the animal was anaemic, with a hematocrit of 27% (reference: 37%-55%). The serum biochemical tests showed urea, creatinine, ALT, and AST values within normal limits, but the cholesterol value was above the reference limits, being 500 mg/dL (reference: 111.9 - 386.1 mg/dL) [11].

Therefore, in view of the physical examination performed on the day of the consultation, the clinical condition of the animal, and the results of the examinations, associated with the lack of a satisfactory



Figure 1. Animal showing the sign of walking in circles on the day of the appointment at the Universidade Estadual de Santa Cruz's Veterinary Hospital (HV-UESC), Ilhéus, BA, Brazil.

response to the prescribed treatment, hypothyroidism was suspected.

Hormonal tests were requested for total T4, free T4 by dialysis and TSH, and the following results were obtained: total T4: 0.3 ng/dL (reference: 1.1-3.6 ng/dL); free T4: 0.15 ng/dL (reference: 0.9-2.6 ng/dL), and; canine TSH: 0.273 ng/mL (reference: 0.08-0.32 ng/mL), confirming hypothyroidism [13].

Considering the results of the hormonal tests, the previously prescribed treatment was suspended, hypothyroidism was confirmed and a new treatment was initiated using thyroxine³ replacement [Levothyroxine - 20 µg/kg, p.o., QD, continuous use]. After 3 days of treatment, the neurological signs regressed, the animal became more active and started to lose weight, and after 30 days, hair regrowth had begun in the areas of alopecia.

Nine months after starting treatment, the animal underwent a new clinical evaluation and blood collection. The dog weighed 47.5 kg, cholesterol was 298 mg/dL, and total T4 dosage was 7.0 ng/dL. Thyroxine was adjusted to 10 µg/kg QD, and a new evaluation of the animal was performed 5 months after this adjustment. At this new evaluation, the animal was clinically well (Figure 2), and the total T4 dosage was 2.5 ng/dL, and within the reference values. Thus, thyroxine³ [Levothyroxine - 10 µg/kg, p.o., QD, continuous use] was maintained as a maintenance treatment.

DISCUSSION

The present report refers to a case of hypothyroidism in a giant dog breed. These breeds are predisposed to the onset of hypothyroidism [10], although the Dogo Argentino breed is not commonly cited in the literature as being associated with this dysfunction. Purebred dogs, as is the case in this report, are more predisposed to the development of hypothyroidism [5]. This disease can affect animals of any breed, since studies have identified certain individual breeds as predisposed over the years. Furthermore, there may be potential variations in the genetic composition of the same breeds in different countries [14].

In this study, the patient was 4-year-old when he was diagnosed with hypothyroidism. This disease affects middle-aged and older animals, with an average age of diagnosis of approximately 7 years [14], which is not corroborated by this case report. The patient was diagnosed at 4 years of age, but the animal was already presenting clinical signs compatible with

hypothyroidism, such as being overweight and the presence of dermatopathy, which reinforces the idea that it was ill well before the time of diagnosis.

The dog in this case report was male and intact. This endocrine disease can affect animals of any sex and neutering is a significant risk factor [14], which was not observed in this case since the animal was intact.

The dog presented dermatological, metabolic, and neurological clinical signs. The clinical signs of hypothyroidism in dogs are nonspecific [9]. This is due to the fact that the thyroid hormone causes a wide variety of physiological effects, with this disease causing changes in many organs [17], which was corroborated in this clinical case.

The main grievances observed in the patient were compulsively walking in circles and a proprioception deficit in all 4 limbs, despite the fact that other researchers [8] state that neurological and muscular signs are rare in hypothyroidism. The case report in question demonstrated neuropathy associated with hypothyroidism, since other diseases were excluded through the blood tests and images that were performed, and by the complete recovery of neurological abnormalities after levothyroxine supplementation.

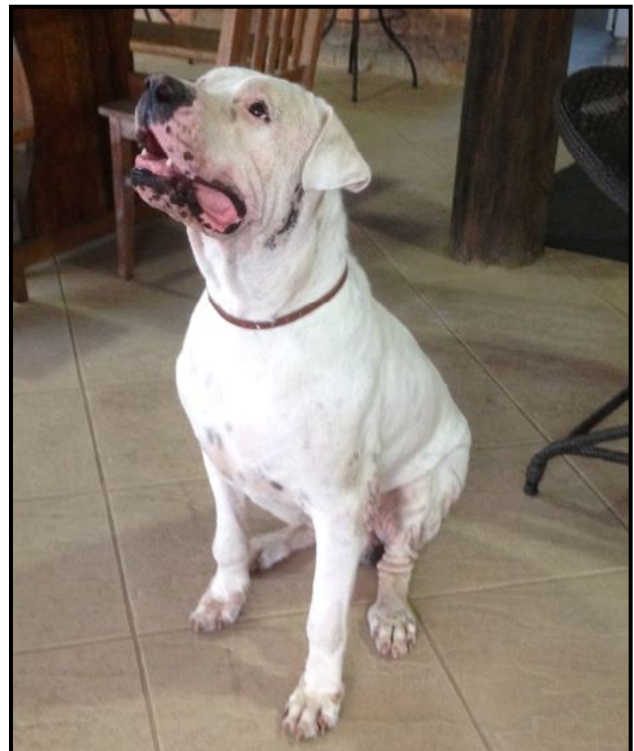


Figure 2. Animal after the diagnosis of hypothyroidism, undergoing hormone replacement.

Regarding the neurological dysfunctions presented by the patient, some reports mention several neurological signs associated with hypothyroidism resulting from involvement of the peripheral nervous system, such as vestibular dysfunction, facial paralysis, reduced spinal reflexes, ataxia, and paresis. It is believed that the neurological dysfunctions that the dog presented in this study were similar to those in other case report [20], with the cause of the changes being the edematous deposition of hyaluronic acid, resulting in compression of nerve fibers. In canine hypothyroid polyneuropathy, both the cranial nerves and the spinal cord may be compromised. The animal in this report displayed ataxia and proprioception deficit in the four limbs due to spinal cord alterations.

Chronic hypothyroidism induced by thyroid irradiation does not result in clinical or electrophysiological evidence of peripheral neuropathy, but causes subclinical myopathy [17]. Some authors have associated this finding with the fact that the animals used were young and medium-sized, since they believe that peripheral neuropathy is more common in older animals, which is not in line with the present study, and that it affects larger animals, which is corroborated by the present study.

The animal in this study was obese, prostrate and lay down all day, which is characteristic of a decrease in metabolic activity with thyroid hormone deficiency. These signs may be present in about 50% of cases [15].

Regarding the dermatopathy, the animal presented symmetrical alopecia in the lateral region of the thighs and tail. Hypothyroid dogs may present alopecia or difficulty growing hair after cutting, in addition to weak hair. This happens because thyroid hormones are responsible for the anagenic phase of hair growth, and hormonal deficiency leads to the permanence of hair in the telogenic or resting phase [19].

Laboratory abnormalities are correlated with the severity and chronicity of the disease. In the present report, the dog presented anemia, which corroborates from the literature, which reports that 25 - 40% of these dogs present mild, normocytic, normochromic, and non-regenerative anaemia [15]. This is due to the decrease in oxygen consumption by the body, which compromises the production of erythropoietin and leads to an increase in the concentration of 2,3-diphosphoglycerate in the erythrocytes. This in turn is related to the affinity of haemoglobin for oxygen and due to

the absence of a direct effect of thyroid hormones in the bone marrow [3]. In addition to anaemia, the dog also presented hypercholesterolemia, an alteration observed in 75% of hypothyroid canines [15]. This is the most common alteration in biochemical tests, even in fasted animals. In this case, it is due to reduced synthesis and degradation of lipids, with lower degradation prevailing. This predisposes the animal to the accumulation of cholesterol and triglycerides in the plasma.

After the results of the blood count and biochemical tests were received, and with suspected hypothyroidism, a thyroid profile was requested for the animal in question. The patient displayed a decrease in total T4 and free T4, which is expected in a hypothyroid animal [16], and presented TSH within the reference values. It is expected that TSH increases with hypothyroidism due to negative feedback generated by the decrease in thyroid hormones. In this report, TSH remained normal, even with decreased levels of total T4 and free T4. However, it is known that up to 38% of dogs with hypothyroidism do not have elevated TSH levels [16], as was the case with this dog.

Evaluating the patient in question, we ruled out the possibility of congenital hypothyroidism. This disorder is rare and often underdiagnosed. The congenital disorder causes a variety of clinical signs, depending on the primary defect. The main signs are mental impairment and skeletal development abnormalities, resulting in disproportionate dwarfism [2]. This was not observed in the animal in question, since it had no problems as a puppy.

Therefore, based on the knowledge that the animal had primary hypothyroidism, it may have been caused by lymphocytic thyroiditis, the most common cause, or by atrophy of the gland. For better elucidation of the case, a test for thyroglobulin autoantibodies (TgAA) could have been performed, but this was not possible because at the time of diagnosis this test was not available in Brazil.

Initially, on the day of the consultation, encephalitis was suspected and enrofloxacin and prednisone were prescribed. However, the animal did not improve with the prescribed medication, since it was not a case of encephalitis. After confirmation of hypothyroidism, levothyroxine was prescribed. The treatment of this endocrine disease should be based on lifetime oral replacement of thyroid hormones, and synthetic T4 (levothyroxine) is the drug of choice [9].

The dog in this report started with thyroxine at a dose of 20 µg/kg QD, which corroborates with literature [9], which recommends an initial dose of 20 µg/kg/QD up to 22 µg/kg/QD. The same author also recommends dividing the daily dose into 2 applications, i.e., 10 µg/kg/BID.

The initial dose from this study was not satisfactory and needed to be readjusted later. This is in line with a study conducted at the Universidade Federal de Guarulhos [4] using 30 dogs that had acquired primary hypothyroidism, treated orally with human levothyroxine sodium. The authors found that there is a large variation in the rate of metabolism and absorption of levothyroxine, which is independent of the weight of the animal. Therefore, for each animal there is an appropriate dose and frequency of levothyroxine administration. Ideally, an initial dose of 15 µg/kg/QD should be given, and after the post-thyroxine test the dose should be adjusted according to the animal's needs [4].

After 3 days of treatment, the patient's neurological signs started improving. According to the literature, after the institution of the correct medication, improvement is rapid. This disorder can be controlled and there is an excellent prognosis [7]. A study states that myopathy due to hypothyroidism responds quickly to thyroid replacement therapy and clinical normalization is achieved within 2 to 8 weeks [20]. On the other hand, when there is peripheral neuropathy, responses to treatment can be poor. The dog in this report showed quick improvement in neuropathy, unlike the dog reported by other researchers [20], which required 6 weeks to observe the first improvement in neurological signs. Therefore, the time required for recovery can be prolonged depending on the severity of nerve involvement.

In general, there was rapid improvement in the clinical signs of the animal in this report. According to the literature, the level of activity and serum cholesterol show rapid improvement after the start of treatment [6], while dermatological signs and body condition, such as being overweight, require a longer period and can take many months [12].

The animal in this report underwent a new hormonal evaluation after 9 months of treatment because the trainer had difficulty in taking the animal to the Veterinary Hospital due to its large size. This first post-therapy hormonal evaluation, revealed that there was a need to adjust the thyroxine dose, since total T4

was above the reference values for the species. The animal showed no signs of thyrotoxicosis. This first post-therapy evaluation was delayed, because monitoring should take place between 4 and 8 weeks after beginning treatment [6]. In addition, monitoring should be performed every 2 weeks until an acceptable dose of total T4 is established [9]. Then, subsequently, the patient should be reassessed every 3 to 6 months, which was also not performed in this case. In the present case, after this first evaluation, it was decided to reduce the dose of thyroxine to 10 µg/kg QD.

The second hormonal evaluation of the animal was also delayed and was only performed 5 months after the dose adjustment. Although the monitoring was not satisfactory, the new dosage showed that the total T4 value was within the normal range. The animal was fine after the dose readjustment, so 10 µg/kg QD was maintained.

The dog in this report presented signs compatible with hypothyroidism and its condition was aggravated by the neurological signs observed, which is rare.

In the present report, the clinical signs and the increase in cholesterol, associated with the results of the hormonal tests, were sufficient for the diagnosis of the disease. With dogs with hypothyroidism, it is necessary to establish an early diagnosis and initiate appropriate treatment to ensure a good prognosis.

In the literature, the dose of thyroxine is quite variable. Therefore, the initial dose caused an increase in total T4, but no clinical signs resulting from this increase were present. Attention should be paid to the initial dose and readjustments made when necessary, which justifies the importance of constant monitoring.

Hypothyroidism should be considered as a differential diagnosis in patients with neurological signs, apathy, and that are overweight. Although neurological changes indicated the progression of the disease in the case reported, when comparing the clinical picture of the affected dog with other cases reported in the literature, it can be concluded that it showed a rapid clinical improvement.

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