

CLINICAL AND NEUROLOGICAL COORDINATES IN THE DIFFERENTIAL DIAGNOSIS OF HYPOTHYROIDISM IN CORRELATION WITH PERIPHERAL NERVOUS SYSTEM DISORDERS - A CASE SERIES REPORT -

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Abstract

Hypothyroidism is a prevalent endocrine disorder in dogs, characterized by a spectrum of clinical manifestations encompassing metabolic, dermatological, reproductive, and neurological abnormalities. In cases where neurological deficits are the sole presentation of hypothyroidism, the diagnostic process is frequently complicated by the overlapping features with peripheral nervous system (PNS) disorders. Notable similarities between these conditions include reduced spinal reflexes, postural changes, generalized muscle weakness associated with atrophy. The objective of this study is to present the diagnostic coordinates of ten canine patients who were presented during 2024 to the Veterinary Emergency University Hospital Prof. Dr. Alin Bîrțoiu in Bucharest with neurologic deficits that imposed differential diagnosis between PNS disorders and hypothyroidism. The protocol used included patient identification, anamnesis, clinical examination, complete neurological evaluation, followed by localization of the lesion and differential diagnosis based on the VITAMIND acronym. Confirmation of hypothyroidism was based on the measurement of serum thyroxine (T4) concentrations.

Key words: hypothyroidism, peripheral nervous system disease, peripheral neuropathy, T4, generalized muscular weakness.

INTRODUCTION

Hypothyroidism is one of the most frequent endocrine disorders diagnosed in canine patients (Graham et al., 2007; O'Neil et al., 2022). Despite its increased prevalence, the polymorphic clinical presentation of this condition may lead the clinician towards dermatologic, metabolic or endocrine pathologies, masking the real etiologic factor (Dixon et al., 1999). The underlying mechanism may be primary (due to lymphocytic thyroiditis or idiopathic atrophy of the thyroid gland) or secondary (due to insufficient secretion of thyroid stimulating hormone - TSH). However, more than 95% of cases occur as a consequence of primary hypothyroidism (Mooney, 2011). Throughout the entire body, an insufficient level of thyroid hormone will decrease the overall rate of metabolism, causing a cascade of effects across multiple organs. Therefore, clinical signs, often variable and progressive, may include excessive fatigue, decreased physical activity,

weight gain or inability to adapt to cold temperatures. These alterations may be accompanied by dermatologic signs, such as bilateral symmetrical alopecia, especially present on the lateral areas of the trunk, lower chest and tail (the so-called "rat tail"). In addition to previously stated signs, there are reports linking primary hypothyroidism with the occurrence of canine polyneuropathy (Tsuboi et al., 2013). This neurological manifestation mimics the characteristic features of a peripheral nervous system (PNS) disorder that includes several syndromes, such as lower motor neuron disease, peripheral vestibular syndrome, laryngeal paralysis or megaesophagus (Rossmeisl et al., 2009). In contrast to the other clinical signs, the mechanisms underlying the triggering of hypothyroid polyneuropathy in dogs have not been elucidated, but same types of lesions that have been evidenced in humans, including mucin deposits that generate demyelination and interfere with axonal transport, are suspected (Shirabe et al., 1975;

Falca et al., 2011). The complexity of hypothyroidism in dogs, arising from the variability and polymorphism of the clinical signs, as well as the insufficient information regarding the polyneuropathy-like expression of the endocrinopathy, require further studies in this direction (Jaggy & Oliver, 1994). Therefore, the present article aims to investigate the main clinical and neurological diagnostic coordinates, through a standard investigation protocol, in a series of ten canine patients in whom thyroid hormone insufficiency led to the onset of polyneuropathy. All dogs included in the study showed at least one neurological deficit, which led to the modification of the classical diagnostic protocol by introducing a complete neurological examination and a neurolocalization, with the aim of differentiating between muscular weakness due to insufficient thyroid hormones and muscular weakness due to a peripheral nervous system disorder.

MATERIALS AND METHODS

The study was conducted between January 2024 and December 2024 and included 10 dogs diagnosed with hypothyroidism at the Veterinary Emergency University Hospital Prof. Dr. Alin Bîrțoiu in Bucharest (Table 1).

Table 1. Main signalment studied features for the 10 patients included in the study

| CANINE | Spitz | M | 12 |
|--------|-------------------|---|----|
| | Yorkshire terrier | M | 12 |
| | Bichon Maltese | F | 5 |
| | Bichon Maltese | M | 11 |
| | German Shepard | F | 6 |
| | Pinscher | M | 11 |
| | Poodle | M | 15 |
| | French Bulldog | M | 6 |
| | Bichon Maltese | M | 5 |
| | Bichon Maltese | M | 6 |

All patients manifested neurological deficits compatible with PNS disorders. The protocol used for examination was based on signalment, history, clinical examination, complete neurological evaluation, followed by

localization of the lesion and differential diagnosis based on the VITAMIND (vascular/inflammatory/trauma/anomaly/metabolic/idiopathic/neoplastic/degenerative) acronym (Dewey & da Costa, 2015). The inclusion criteria centred on the clinical manifestation characterized by general muscular weakness (ranging up to tetraparesis) correlated with low T4 concentrations and an elevated TSH value in the biochemical blood test. The measurement was realised using immunochemistry with electrochemiluminescence (ECL) detection (Dixon & Mooney, 1999; Fernoagă & Turbatu, 2023). All ten patients were radiologically assessed to rule out megaesophagus. The obtained data were manually collected and revised from the Consultation Register. The analysis regarding significant information about signalment, clinical abnormalities and neurological deficits will be discussed in the following sections.

RESULTS AND DISCUSSIONS

According to the protocol implemented in the Hospital, the analysed elements from the patient's signalment were breed, age and sex, with the aim to correlate them with the existing data in the literature regarding the predisposition of certain canine patients to develop hypothyroidism. Relating to breed, it should be mentioned that all dogs belonged to a pure breed (n=10, 100%), with a higher prevalence of Bichon Maltese breed (n=4) compared to the other breeds, as shown in Figure 1.

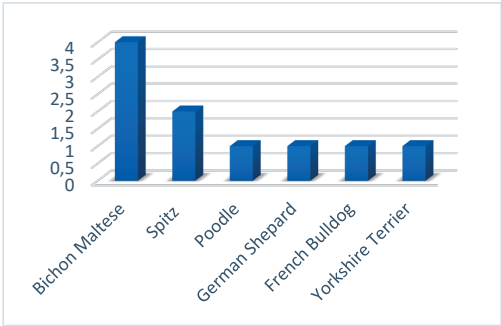


Figure 1. Distribution of patients according to breed

Previous studies have shown that certain breeds like Schnauzer, English Setter or Dunker have

an increased risk of developing hypothyroidism (Ringstad et al., 2022). However, none of the patients included in the study belonged to these breeds.

The second investigated element was the sex of the patients. Out of the 10 dogs, 80% (n=8) were males and 20% were females (n=2), the percentage of sterilized animals being 100% (n=10). Previous articles that have studied the impact of gender on the onset of hypothyroidism have shown that males and females are equally affected by this endocrinopathy. However, neutered animals appear to be at higher risk, which has also been confirmed by the group of patients included here (O'Neil et al., 2022).

The distribution of patients according to age (as shown in Figure 2) confirmed the results previously proven by other studies, according to which acquired hypothyroidism occurs at an older age. Thus, the mean age in the population (n=10) was 9 years, the youngest patient was 5 years old and the oldest 15 years old. Other similar articles have emphasized that this endocrinopathy affects middle-aged animals and geriatric animals, the mean age previously reported being approximately 7.5 years (Dixon & Mooney, 1999).

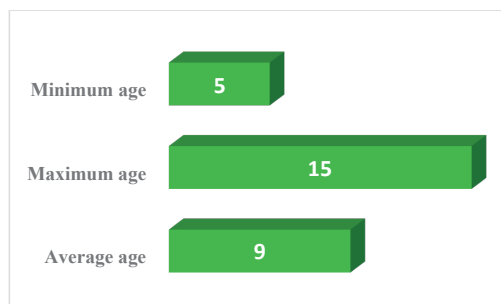


Figure 2. Distribution of patients according to age (n=10)

Anamnesis revealed a series of common clinical signs for patients diagnosed with hypothyroidism, such as unstable or swaying gait accompanied by progressive muscle weakness that evolved to the point of permanent recumbency, effort intolerance, decreased appetite, but doubled by an increased weight, change in the appearance of the coat by the development of areas of bilateral alopecia. The diagnostic protocol consisted of assessing all patients through a clinical examination that included auscultation of the heart and

respiratory system, palpation of explorable lymph nodes, abdomen and thyroid.

The symptomatology recorded at this assessment stage confirmed the anamnesis data, such as the presence of skin and fur lesions (Figure 3 A and B), changes in general condition and body score, difficulty in moving or inability to leave the recumbency (Figure 4).

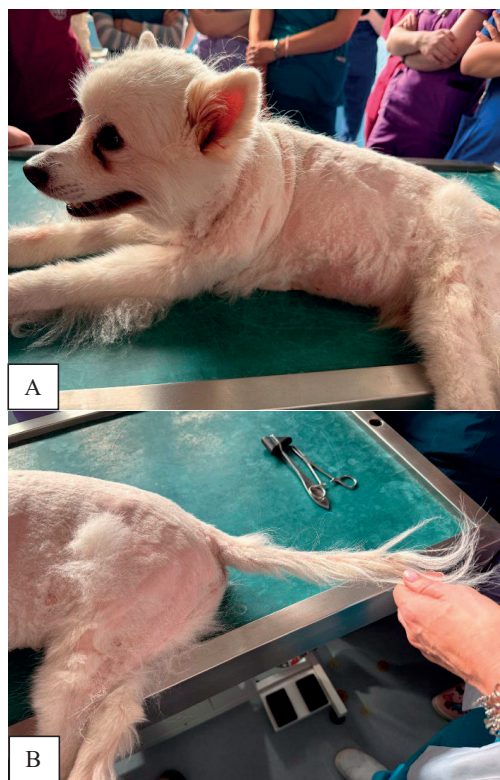


Figure 3. Specific dermatologic lesions of hypothyroidism in a Spitz dog - bilateral symmetrical alopecia of the trunk (A) and rat tail (B)



Figure 4. Generalized muscular weakness and permanent decubitus in a Yorkshire terrier male with hypothyroidism

The 10 patients selected for this study developed, in addition to metabolic or dermatologic signs, at least one neurologic deficit. Therefore, their evaluation included a complete neurological examination, which was completed with neurolocalization of the lesions and differential diagnosis between central and peripheral nervous system dysfunction. The stages of the neurological examination included assessment of mental status, behaviour, cranial nerves, posture, gait, postural reactions, spinal reflexes and sensitivity.

The most common deficits recorded in the neurological examination were - depressed mental status, permanent decubitus and generalized muscle weakness, inability to walk, proprioceptive deficits and reduced spinal reflexes on all four limbs (Figure 5 A and B).



Figure 5. Inability to maintain standing position, proprioceptive deficits (A) and reduced spinal reflexes on all limbs (B) in a male Yorkshire terrier with hypothyroidism

Considering the presence of acquired polyneuropathy, in all 10 patients the neurolocalization was oriented towards a peripheral nervous system (PNS) disorder. The differential diagnosis was made following the acronym VITAMIND and aimed to exclude infectious (*Neospora caninum*, *Clostridium botulinum*,

Toxoplasma gondii, *Hepatozoon canis*, *Leptospira interrogans*, *Dirofilaria immitis*), autoimmune (*Lupus erythematosus*), congenital (breed specific), metabolic (*Diabetes mellitus*, hypothyroidism, hypokalaemia) or paraneoplastic diseases (lymphoma, thymoma) (Musteață et al., 2022). However, considering the correlation of the anamnesis with the absence of genetic predisposing factors and the associated clinical signs, all patients underwent the determination of blood T4 concentration values. As part of the protocol, for all dogs underwent thoracic radiographs were performed, in order to rule out the presence of megaesophagus, commonly associated with peripheral nervous system disorders (Musteață et al., 2022).

The results of the biochemical analysis confirmed the presence of hypothyroidism, by correlating low T4 values (below 1.5 ug/dL) with elevated TSH values (above 0.5 ug/dL).

CONCLUSIONS

Hypothyroidism is a commonly diagnosed endocrinopathy in dogs. However, the evolution in the form of polyneuropathy is accompanied by neurological deficits that often lead to difficulties in diagnosis.

For a correct diagnosis, the implementation of a protocol that includes patient signalment, anamnesis, clinical examination, neurological examination (for polyneuropathy cases), laboratory blood tests and thoracic radiographs is mandatory.

In the present study, there was no evidence of a race predisposition, but all patients belonged to the susceptible age categories for developing primary hypothyroidism (mean age 7.5 years).

The most common clinical signs associated with hypothyroidism were gait instability, generalized muscle weakness, bilateral alopecia and obesity. All patients showed a reduction in spinal reflexes, which led to the diagnosis of a peripheral nervous system disorder

Among the 10 patients included in the study, no patient had megaesophagus following radiologic evaluation.

For all cases, low T4 concentrations were correlated with high levels of TSH.

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