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Popular Article

Nervous Manifestation of Hypothyroidism in Dogs

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Abstract

Hypothyroidism, a prevalent endocrine disorder in dogs, results from inadequate thyroid hormone production by the thyroid gland, leading to a diverse range of clinical manifestations. This article delves into the neurological and behavioral implications observed in dogs affected by hypothyroidism. While numerous cases have been documented, the precise etio-pathogenesis remains elusive. Our objective is to comprehensively elucidate the correlation between hypothyroidism and nervous/behavioral symptoms, providing a convincing and informative analysis.

Key words: Hypothyroidism, Neurological/ Behavioural signs, Correraltion.

Introduction

Hypothyroidism, a prevalent endocrine disorder in canines, stems from a deficiency of active thyroid hormones, namely triiodothyronine (T3) and thyroxine (T4) (Mooney, 2011)[14]. The origins of hypothyroidism can occur due to functional abnormalities in the Hypothalamus, Pituitary gland, and Thyroid gland. However, a substantial 95% of reported cases are associated with lymphocytic thyroiditis or idiopathic atrophy of the thyroid gland (Mooney, 2011)[14]. Certain breeds are highly susceptible to hypothyroidism like beagles, boxers, pointers, golden retrievers and labrador retrievers (Fors, 2006)[6]. A variety of clinical signs are recorded in hypothyroidism including classical dermatological signs (non-pruritic alopecia, obesity, lethargy), some rare neurological signs (ataxia, paraparesis, vestibular syndrome, facial paralysis, etc.) and behavioural

signs. It is noteworthy that the dog may not show any classical dermatological signs while showing nervous signs (Foss, 2006)[6].

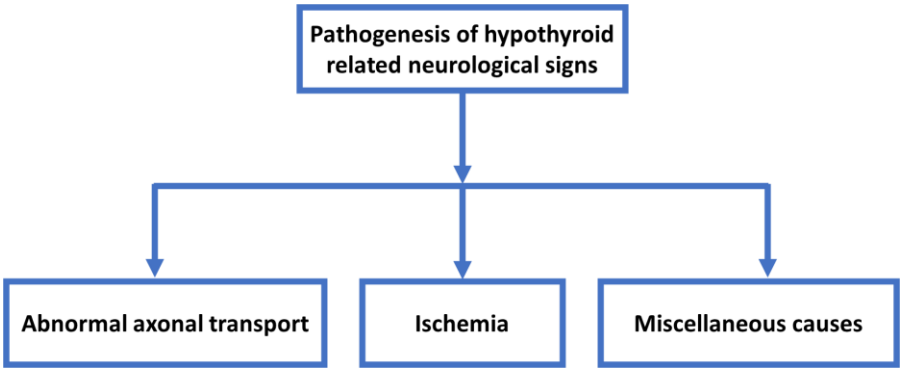
Pathophysiology of Hypothyroidism Related Neurological Signs

Among all the dogs suffering from hypothyroidism, about 7.5% are recorded having neurological signs (Blois, 2008)[2]. Any definite relationship between hypothyroidism and neurological dysfunctions is not established, however some pathophysiologic mechanisms may involve in development of neurological signs, i.e. (Bertalan *et al*, 2013)[1].

1. Abnormal axonal transport
2. Ischemia
3. Miscellaneous causes

Abnormal Axonal Transport

Hypothyroidism causes decrease in ATPase activity, leads to decreased activity of Na^+/K^+ pump. Additionally, hypothyroidism leads to altered microtubule formation and axonal degeneration leads to development of neurological signs (Dewey, 1995)[4].



Ischemia

In hypothyroid animals, the reduced thyroid function contributes to tissue ischemia and subsequent infarction, leads to development of atherosclerosis. Atherosclerosis is marked by the thickening of the Tunica media/interna of arterial walls, accompanied by elevated levels of lipids and lipid deposition. This cascade of events results in neuronal degeneration. (Hess, 2003)[7].

Miscellaneous causes (Bertalan, 2013)[1]

1. Secondary immune-mediated demyelination of nerves.
2. Deposition of glycogen around nerves.
3. Lipid granulomas.

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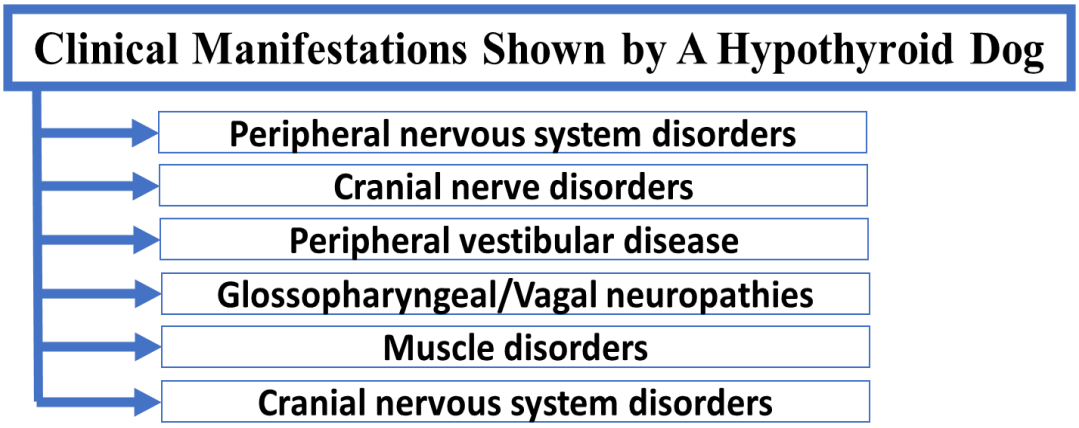
Clinical Manifestations Shown by A Hypothyroid Dog



Peripheral Nervous System Disorders

The most common neurologic disorders related to hypothyroidism is neuropathy and myopathy:

1. Generalized Polyneuropathy

Hypothyroidism is linked to polyneuropathy, characterized by conditions such as pelvic limb paresis, tetraparesis, hyporeflexia, hypotonia, and muscular atrophy. Larger dog breeds, including Labrador, Golden Retriever, and German Shepherd, exhibit a higher susceptibility to polyneuropathy (Bertalan, 2013)[1].

The diagnosis of hypothyroid-induced polyneuropathy involves documenting neuro-muscular dysfunction (Bertalan, 2013)[1]. For a conclusive diagnosis, Electromyography (EMG) proves valuable. EMG can detect fibrillation potentials, increased insertional activity, and complex repetitive discharges from muscles (Scott-Moncrieff, 2007)[20]. Additionally, histopathologic examination of nerve tissue, revealing Wallerian degeneration neuropathy, provides a diagnostic avenue (Roxanis, 2002)[19].

2. Myasthenia Gravis

In humans, there are many evidences of hypothyroidism associated with myasthenia gravis. About 10% to 20% of people suffering from myasthenia gravis are having history of hypothyroidism (Levine, 2005)[11].

Hypothyroidism associated myasthenia gravis is also seen in dogs. According to hypothesis of (Dewey, 1995)[4], the auto-antibodies of acetylcholine (Ach) receptor cross-react with self-antigens in thyroid gland.

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Cranial Nerve Disorders

Neuropathies affecting multiple cranial nerves, including the facial nerve, vestibulocochlear nerve, and trigeminal nerve, have been observed in dogs (Bertalan, 2013)[1]. In a study conducted by Panciera in 2001[16], approximately 70% of dogs with hypothyroidism exhibited facial paralysis, accompanied by additional signs such as lip droop, ear droop, and decreased tear production.

The likely cause of facial neuropathies in these cases is the presence of myxedematous deposits surrounding the facial nerves (Panciera, 2001)[16]. Additionally, decreased vascular perfusion has been identified as a contributing factor to facial paralysis (Vitale, 2007)[22].

Peripheral Vestibular Disease

Peripheral vestibular syndrome may manifest as a secondary condition to hypothyroidism. Clinical symptoms associated with peripheral vestibular syndrome include an ipsilateral head tilt, vestibular ataxia, circling, ipsilateral ventral strabismus, and horizontal nystagmus. Postural reactions and spinal reflexes may remain normal (Cuddon, 2002)[3].

In most reported cases, the onset of clinical signs is acute and non-progressive. However, in some instances, the disease course can be chronically progressive. Vestibular symptoms linked to hypothyroidism-associated neuropathy often exhibit complete or partial reversibility within two to four months with the administration of thyroid hormone supplementation therapy (Fors, 2006)[6].

Glossopharyngeal/Vagal Neuropathies

1. Laryngeal Paralysis.

In a study involving 140 dogs afflicted by laryngeal paralysis, hypothyroidism was reported in approximately 21% of cases (MacPhail, 1985-98)[12]. Another study, which examined 66 dogs, identified 2 cases with hypothyroidism (Panciera, 2001)[16].

It is noteworthy that the treatment for laryngeal paralysis is primarily surgical, and mere levothyroxine supplementation is not considered a viable therapeutic approach (Fors, 2006)[6].

Muscle Disorders

Hypothyroidism in dog's manifests as skeletal muscle pain, stiffness, and generalized weakness, leading to an inability to bear weight without assistance (Rossmeisl, 2009)[19].

The development of myopathy in hypothyroidism is attributed to a reduced level of carnitine, a vital component for beta-oxidation in mitochondria. This decline may result from the decreased synthesis of "novo carnitine," leading to the release of carnitine from skeletal muscles into the extracellular compartment and subsequent excretion through urine. Consequently, affected

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dogs exhibit higher levels of urinary carnitine and lower levels of muscle carnitine. (Rossmeisl, 2009)[19]

Hypothyroidism-induced peripheral nerve dysfunction is believed to stem from several mechanisms. These include disruptions in standard carbohydrate metabolism, an increase in slow myofibrillar proteins, irregularities in oxidative phosphorylation, abnormalities in triglyceride turnover, and unusual cation transfer across the sarcolemma. (Dewey, 1995)[4]

Central Nervous System Disorders

Hypothyroidism has been linked with various clinical symptoms, including mental dullness, circling behavior, seizures, and central vestibular signs, as well as cognitive dysfunction (Vitale, 2007)[22]. These symptoms may be caused by several mechanisms, such as atherosclerosis, myxedema coma, or the presence of a pituitary tumor. Despite the metabolic effects of decreased T4 levels, the Central Nervous System (CNS) tends to be resilient. As a result, CNS dysfunction is a rare occurrence in hypothyroid dogs and is typically associated with ischemic pathology (Bertalan, 2013)[1].

1. **Central Vestibular Disease**

This includes a variety of clinical signs including abnormal nystagmus, postural reaction defects, tetraparesis/hemiparesis and paradoxical central vestibular dysfunction (head tilting). (Higgins, 2006)[8]

2. **Prosencephalic Signs**

These are characterized by propulsive circling, seizures, behavioural changes (aggression and dementia) (Scott-Mocrieff, 2007)[20]. Stupor and coma, also known as Myxedema coma, also can occur due to hypothyroidism (Feldman, 2004)[5].

Pituitary neoplasms, that causes secondary hypothyroidism, also gives neurological signs, including ataxia, seizures, depression and head pressing (Patterson, 1985)[17].

CASE HISTORY RECORDS

1. **Neurological signs of hypothyroidism: a retrospective study of 29 dogs (Jaggy *et al*, 1994)[9]**

In this study many nervous signs associated with hypothyroidism were described in 29 dogs, where 11 have motor neuron signs, 9 had peripheral vestibular deficits, 4 suffering from megaesophagus, and from laryngeal paralysis. All these dogs were diagnosed with hypothyroidism and responded towards levothyroxine supplementation.

2. **Hypothyroidism in a Boxer Dog (McKeown, 2002)[13]**

McKeown reported a case of a boxer dog showing signs of head tilt, facial paralysis,

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excessive drooling, drooping of left ear, eyelid and lip. The dog was found suffering from hypothyroidism and responded to given levothyroxine supplementation.

3. **Central nervous system atherosclerosis in Australian Shepherd dog. (Blois*et al*, 2008)[2]**

A study of 2-year-old, castrated male Australian Shepherd was presented with a history of chronic mild ataxia, obesity, and lethargy. Despite treatment with levothyroxine, the ataxia exacerbated. Subsequently, cranial nerve abnormalities surfaced, leading to the difficult decision to euthanize the dog. Postmortem examination unveiled significant thyroid gland atrophy and widespread, severe atherosclerosis within the central nervous system.

4. **Neurologic Dysfunction in hypothyroid/hyperlipemic labrador. (Vitale &Olby, 2008)[23]**

Three Labrador Retrievers and one Labrador Retriever cross met the inclusion criteria for this study. All of these dogs were diagnosed with hypothyroidism and exhibited severe hyperlipidemia. Neurological manifestations included tetraparesis, central and peripheral vestibular signs, facial paralysis, and paraparesis.

Among the observed cases, two dogs presented with an acute onset of symptoms and demonstrated a swift resolution, suggestive of an infarct. Magnetic resonance imaging confirmed the presence of an infarct in one of these dogs. Additionally, two dogs displayed chronic histories of cranial neuropathies and paraparesis. Notably, one of these dogs exhibited evidence of iliac thrombosis and atherosclerosis upon ultrasound examination. Importantly, all dogs exhibited improvement with thyroid hormone supplementation.

5. **Histopathological study on hypothyroid dogs (Rossmeisl, 2009)[19]**

In this study it was reported that dogs suffering from hypothyroidism shows muscular atrophy and a decreased type II : type I myofiber area ratio compared to control dogs. It was also reported that hypothyroid dogs have increased carnitine levels in urine and decreased muscle carnitine level than control dogs.

6. **Hypothyroidism in a Labrador dog (Vaishali & Tushar, 2019)[21]**

In this study a Labrador dog was reported with signs of cold intolerance, facial paralysis and stridor from Laryngeal paralysis. On blood T4 and TSH examination, the dog was found to be hypothyroid. On thyroxine therapy all these nervous signs resolved.

7. **Hypothyroidism in 4 yr old Labrador (Kachhawa*et al,* 2021)[10]**

In this case a dog was reported suffering from progressive ataxia, inability to bear weight on limbs and on lateral recumbency. The dog was found positive for hypothyroidism associated neuropathy as its thyroid profile test revealed a marked decreased in T3, T4 level and elevated TSH. The dog

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showed remarkable recovery in 15 weeks with levothyroxine-sodium therapy.

8. Hypothyroidism in a Dogo Argentino dog (Oliviera *et al,* 2022)[15]

In this study an Argentino dog was reported with clinical signs of walking in circles and lack of proprioception in the limbs. These signs readily subside by thyroxine therapy.

Conclusion

The intricate relationship between primary hypothyroidism and various neurological manifestations in dogs, encircling lower motor neuron disease, peripheral vestibular syndrome, facial paralysis, laryngeal paralysis, megaoesophagus, and myasthenia gravis, continues to be an area of active exploration. While the link between hypothyroidism and polyneuropathy, as well as peripheral vestibular syndrome, is well-supported by consistent findings in electrodiagnostic testing and muscle and nerve biopsies, the associations with facial paralysis, laryngeal paralysis, megaoesophagus, and myasthenia gravis remain less clear.

Confirmation of hypothyroidism-induced neurological manifestations relies on a multifaceted approach, including clinical observation of neurological signs, clinicopathologic findings such as low T4 concentrations and elevated TSH concentrations, diminished response to TSH-stimulation, as well as results from electrodiagnostic investigations and biopsies of muscles and nerves. While thyroxine supplementation proves efficacious in many cases of polyneuropathy and peripheral vestibular syndrome, its effectiveness diminishes in addressing laryngeal paralysis and megaoesophagus.

Furthermore, it is crucial to recognize the insidious nature of hypothyroidism, characterized by slow and progressive development, often remaining unnoticed. Nervous signs, in particular, may manifest without classical hypothyroidism signs, leading to potential underdiagnosis or misdiagnosis. This underscores the importance of heightened awareness among clinicians, emphasizing the need for thorough assessments and considerations of hypothyroidism in cases exhibiting neurological symptoms, even in the absence of classical manifestations.

In conclusion, hypothyroidism and neurological conditions in dogs are intricate and interconnected aspects of veterinary medicine. Despite of the ongoing debate over the definitive cause-and-effect relationship between thyroid hormone deficiency and neurological changes, the combination of clinical experiences, extensive case reports, and research findings in the literature strongly suggests a significant association. Recognizing the multifactorial nature of thyroid level regulation and the complexity of identifying underlying causes of neurologic syndromes, it is imperative for future studies to delve into the molecular basis of neurologic diseases in hypothyroid

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dogs. Comprehensive investigations into the effects of thyroid hormone deficiency on the peripheral nervous system, central nervous system, and muscles are crucial. While skepticism persists, a thorough understanding will emerge when alternative causes of neurologic dysfunction are meticulously ruled out, potentially necessitating the induction of hypothyroid states for research purposes. Until then, clinicians should remain vigilant to the potential association and consider screening for and treating hypothyroidism in dogs presenting with neurological diseases and clinical signs suggestive of hypothyroidism.

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