

Hypothyroid associated polyneuropathy in dogs: Report of six cases

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Abstract

Six Doberman Pinscher, between six and eight years of age, were presented to the Veterinary Hospital from Faculty of Veterinary Science of The University of Buenos Aires. Neurological examination revealed tetraparesis with inability to walk, decreased muscle tonus and myotatic reflexes in all dogs. Serum cholesterol levels, creatine kinase and alkaline phosphatase activities were mildly to markedly elevated, and tibial motor nerve conduction velocities were slow in all dogs. Basal measurements of free T4 and TSH were determined by radioimmunoassay. Although fT4 values were within normal range, in all dogs TSH values were elevated. Based on this results, hypothyroidism was diagnosed and a supplementation therapy was established with oral levothyroxine (T4). Two weeks after treatment has been started, all patients had an improvement in clinical signs, and within a month gait became normal, as well as muscular tonus and spinal reflexes.

Key words:

Thyroid hormones.
Motor nerve
conduction velocity.
Neuropathy.

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Introduction

Hypothyroidism is the most common endocrine disorder of the dog and is characterized by various cutaneous and noncutaneous clinical signs associated with a deficiency of thyroid hormone activity. Canine hypothyroidism may be naturally occurring or iatrogenic. Naturally occurring acquired primary form accounts for more than 90% of all cases of canine disease. The two main causes of this form are lymphocytic thyroiditis and idiopathic thyroid degeneration (necrosis and atrophy). Lymphocytic thyroiditis is thought to be an autoimmune disorder in which humoral and cell-mediated autoimmunity are involved in the pathogenesis.^{1,2} Anti-thyroglobulin antibodies are demonstrable in the sera of more than 50% of dogs with naturally occurring hypothyroidism and Doberman pinschers appears to be predisposed.^{1,2,3}

The clinical signs associated with hypothyroidism are many and varied and involve multiple organ systems. Although

lethargy, mental depression, slow heart rate, obesity, hypothermia and thermophilia are classic manifestations of hypothyroidism, many dogs appear active and alert, are thin and do not exhibit heat-seeking behaviour.^{3,4,5} Dermatological changes occur in 60 to 80 per cent of hypothyroid dogs.^{3,6} The classic cutaneous signs include bilaterally symmetric truncal alopecia, which tends to spare the extremities; a dull dry brittle, easily epilated haircoat; thick, puffy, nonpitting skin (mixedema) that is cool to the touch; variable hyperpigmentation; seborrhea and susceptibility to skin infections.^{3,4}

The veterinary literature includes large lists of noncutaneous abnormalities associated with hypothyroidism. Aside from mental dullness, central nervous system signs are rare in primary hypothyroidism and can be caused by atherosclerotic or myxedematus changes.^{7,8} The atherosclerotic changes are secondary to hyperlipidemia and can also affect the vessels of the heart, kidneys, and gastrointestinal tract. Signs can include seizures, disorientation, circling and coma. Most cases

have been reported in Doberman pinschers.⁴

A subclinical myopathy has been reported in mature dogs with primary hypothyroidism.^{9,10} Occasionally, signs of neuromuscular disorders can occur with or without cutaneous signs, and these include weakness, stiffness, decreased conscious proprioception and muscle wasting.^{3,10,11} The etiopathogenesis of this endocrine myopathy is unknown. A disturbance in carbohydrate metabolism has been proposed to explain the preferential type II fiber atrophy, which occurs in humans and canine muscle.^{10,11}

A hypothyroid-associated neuropathy does appear to exist in mature to middle-aged dogs, usually in large breeds, and may be recognized without the usual signs of hypothyroidism.^{3,12,13} Peripheral neuropathies may also affect the cranial nerves causing abnormalities such as head tilt, facial nerve paralysis, strabismus, nystagmus, decreased facial sensitivity and laryngeal paralysis.^{3,7,14,15,16,17,18,19} Although the pathogenesis of this neuropathy is not clear, metabolic alterations would determine abnormalities in the transport axonal and in the functionality of Schwann cells.^{3,7} The early stages are often missed because the signs are mild.¹³ The occurrence of megaesophagus, intermittent lameness, paraparesis and tetraparesis have all been associated with hypothyroidism.^{14,15,18,19,20} Clinical signs such as progressive weakness, muscle atrophy (mainly appendicular), hypotonia and depressed spinal reflexes may be seen.^{11,17} Nerve fibers studies are characterized by both demyelination-remyelination and axonal necrosis. Electrodiagnostic studies have revealed multifocal patterns of fibrillation potentials, positive sharp waves and decreased motor nerve conduction velocity.^{3,11} This clinical signs usually resolve with L-thyroxine (T4) supplementation. Dogs improve rapidly within a few days after the start of treatment, and most dogs are neurologically normal after one to two months of treatment.³ In some animals there is a lack of correlation between the degree of electromyographic abnormalities and the severity of

clinical signs.²⁰

Results of hemogram, biochemical panel and urinalysis may support a diagnosis of hypothyroidism and rule out other diseases. A mild nonregenerative anemia and fasting hypercholesterolemia occur in 30 and 75 per cent of hypothyroid dogs, respectively. Less common abnormalities include mild increases in alkaline phosphatase, alanine aminotransferase and creatine kinase.⁶

Despite the routine a regular use of thyroid function tests in veterinary medicine, the practitioner is still plagued with the problem of making an accurate diagnosis of hypothyroidism. While in primary hypothyroidism TSH levels should increase to stimulate the glands to produce more hormone, in secondary or tertiary hypothyroidism levels are low. Because the majority of hypothyroid dogs have primary disease, elevated TSH levels are to be expected in most of them. To increase the discriminating value of TSH, it has been suggested that the assay be run in conjunction with TT4 or free T4 (fT4). In hypothyroidism the TT4 or fT4 would have to be low.^{4,21} Because not all laboratories may use the same assay kit or technique to determine their results, normal ranges can vary from laboratory to laboratory. Values of TSH less than 0,5 ng/ml and from fT4 varying from 0,3 to 1,7 ng/dl are considered diagnostic of hypothyroidism.⁴ The present report concerns six cases of hypothyroid-associated polineuropathy in Doberman Pinscher.

Case Reports

Six Doberman Pinscher (two males and four females), between six and eight years of age, were presented to the Veterinary Hospital from Faculty of Veterinary Science of The University of Buenos Aires with diagnosis of Wobbler syndrome. According to the owners, the diagnosis was made based on clinical signs and radiological studies of cervical column with lateral incidence and in forced flexion of the neck. The problem has progressed slowly, varying from one to three

months and, according to the owners, no one had thermophilia. Three females had altered estrous cycles. All of the dogs received dexamethasone without clinical improvement in any of them. Physical examination revealed rectal temperature within the normal range and normal skin in all dogs. Only a male and a female were presented with obesity. Neurological examination revealed tetraparesis with inability to walk, decreased muscle tonus and myotatic reflexes in all dogs. Two of them also presented disфония.

Complete blood counts (CBC) and biochemical analysis were performed in all dogs. CBC, blood glucose concentrations, total protein, albumin, total calcium, urea nitrogen and creatinine concentrations as well as plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity were within normal ranges in all dogs. Serum cholesterol levels were elevated in all dogs, with values ranging from 292 to 504 mg/dl (Table 1). Serum creatine kinase and alkaline phosphatase activities were mildly to markedly elevated in all dogs, with values ranging from 160 to 1450 U/L and from 180 to 460 U/L, respectively (Table 1).

All dogs were submitted to electroneurographic examination of the tibial nerve. Tibial motor nerve conduction velocities were slow in all dogs, varying from 20 to 38m/s, when compared with normal

dogs, which have velocities higher than 60 m/s.^{22 23,24,25,26}

As the signs were compatible with hypothyroidism, basal measurements of free T4 and TSH were determined by radioimmunoassay using veterinary kits. Although four from six dogs had fT4 values within normal range, in all dogs TSH values were elevated (Table 1). Based on this results, hypothyroidism was suspected and a supplementation therapy was established with oral levothyroxine (T4), adjusting the dose according to each patient's evolution, to confirm the diagnosis. Two weeks after treatment has been started, all patients had an improvement in clinical signs, and within two months thyroid function tests became normal, as well as gait, muscular tonus and spinal reflexes.

Discussion

All dogs presented to the Veterinary Hospital had decreased muscle tonus and myotatic reflexes in the four limbs, suggesting lower motor neuron involvement. Many diseases may cause signs of lower motor neuron involvement and, among them, polyneuropathy associated with hypothyroidism which can be observed in Doberman Pinschers. Peripheral neuropathy is the best documented neurologic manifestation of hypothyroidism. Dogs

Table 1 - Blood chemical data (serum cholesterol levels, creatine kinase and alkaline phosphatase activities), tibial motor nerve conduction velocities and free T4 (fT4) and TSH basal measurements, in six Doberman Pinscher suspected of having hypothyroid-associated neuropathy. Buenos Aires, 2007

Patient	Serum cholesterol (mg/dL)	Serum creatine kinase (U/L)	Serum alkaline phosphatase (U/L)	Tibial MCV (m/s)	fT4 (ng/dl)	TSH (ng/ml)
Dog 1	386	220	190	20	3.2	1
Dog 2	504	1.300	460	38	1.9	1.6
Dog 3	430	1450	250	34	2.8	1.8
Dog 4	292	160	180	25	2.2	2.1
Dog 5	416	850	370	32	1.2	0.9
Dog 6	391	210	230	27	1.1	0.8

typically present with exercise intolerance, generalized weakness, ataxia and quadriparesis or paralysis. There is normally a slow progression of clinical signs from mild gait deficits to paraparesis or tetraparesis observed in most dogs. Neurologic examination typically reveals proprioceptive deficits of the pelvic and thoracic limbs, and diminished segmental reflexes. Most commonly all four limbs are affected; however, in some dogs, clinical signs progress from the hind limbs to the forelimbs or affect the hind limbs alone.³ Dysfunctions of multiple cranial nerves have been reported in hypothyroid dogs, and were observed in the two dogs with disfonía.

Early reports suggested an association between hypothyroidism and cervical spondylomyelopathy, but this association is likely the result of a similar breed predisposition for both disorders. Although cervical spondylopathy (Wobbler syndrome) is a neurologic disorder that appears with great frequency in Doberman pinschers, the disease does not cause lower motor neuron involvement. In most Doberman pinschers clinical signs develop between three and eight years of age. They typically develop mild pelvic limb ataxia that progresses to severe bilateral ataxia and hypermetria. Ataxia and paresis in the thoracic limbs may be pronounced in some cases but are sometimes detected only by careful neurologic examination. Some dogs have tetraparesis.

Neurologic examination evidences upper motor neuron signs in the pelvic limbs (increase muscle tonus and normal or exaggerate myotatic reflexes), and some tetraparetic dogs may have lower motor neuron signs in the thoracic limbs because of cervical gray matter involvement. The diagnosis of cervical spondylopathy is confirmed by survey radiographs and myelography.

All of the six examined dogs had elevated serum cholesterol levels, creatine kinase and alkaline phosphatase activities, besides slow tibial motor nerve conduction velocities which led us thought that hypothyroidism was the cause of the polyneuropathy, suggested by hormonal determinations. It should be kept in mind that many affected animals do not have obvious signs of hypothyroidism. There are several factors that make it hard to determine the true relation between hypothyroidism and many of the less common clinical associations attributed to the disease. One factor is the challenge of confirming a diagnosis of hypothyroidism in dogs. Diagnosis of hypothyroidism is hampered by the lack of specificity of the thyroxine assay as well as the lack of sensitivity of the thyrothrin assay. In many cases it is difficult to make a definitive diagnosis and a therapeutic trial is necessary. In the present cases we confirmed hypothyroidism with therapeutic diagnosis.

Polineuropatia associada a hipotireoidismo em cães: Relato de seis casos

Resumo

Seis Dobermans Pinscher, entre seis e oito anos de idade, foram encaminhados ao Hospital Veterinário da Faculdade de Ciências Veterinárias da Universidade de Buenos Aires. O exame neurológico revelou tetraparesia com incapacidade para andar, diminuição do tono muscular e de reflexos miotáticos em todos os cães. Os níveis de colesterol, creatina quinase e fosfatase alcalina encontravam-se de moderada a acentuadamente elevados. As velocidades de condução nervosa do nervo tibial estavam diminuídas em todos os cães. Os níveis séricos basais de T4 livre e TSH foram determinados por radioimunoensaio e, embora os valores de T4 livre estivessem dentro dos limites de normalidade, em todos os cães o TSH estava elevado.

Palavras-chave:

Hormônios tireoidianos.
Velocidade de condução nervosa motora.
Neuropatia.

Baseado nestes resultados, diagnosticou-se hipotireoidismo e iniciou-se uma suplementação oral com levotiroxina (T4). Duas semanas após o início do tratamento todos os pacientes tiveram melhora clínica e, dentro de um mês a locomoção, o tono muscular e os reflexos medulares tornaram-se normais.

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