A LOOK AT CANINE HYPOTHYROIDISM

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Isabelle Cattin, Jordi Puig discuss approaches to treating this condition, in particular with reference to the primary form, and look at risk factors and clinical signs

HYPOTHYROIDISM can be classified as primary, secondary, tertiary and congenital.

This article will mainly focus on the primary form, as it is the most commonly seen in dogs (more than 95 per cent of cases). Secondary hypothyroidism (thyroid-stimulating hormone [TSH] deficiency) is rarely diagnosed and tertiary hypothyroidism has not yet been described in dogs. Similarly, congenital hypothyroidism (cretinism) has a very low prevalence.

Aetiology and histopathology

Two histologic forms of primary hypothyroidism are predominant: lymphocytic thyroiditis and idiopathic atrophy. Both forms eventually result in progressive destruction of the thyroid gland and deficiency of circulating thyroid hormones.

Lymphocytic thyroiditis is an immune-mediated condition characterised by a diffuse infiltration of mononuclear cells (lymphocytes, plasma cells and macrophages) within the thyroid gland. The result of this inflammation is the progressive destruction of follicles and secondary fibrosis. Clinical signs might not become evident until at least 75 per cent of the gland is destroyed. The immunemediated origin is supported by the increased incidence of circulating autoantibodies to thyroid antigens, like thyroglobulin, T3 and T4. Anti-thyroglobulin antibodies are present in 36 to 50 per cent of dogs with thyroiditis, and their incidence varies greatly between breeds (Ettinger, 2000). Thyroiditis is inheritable in beagle and borzoi breeds (Benjamin, 1996; Conaway, 1985). Idiopathic

atrophy is represented histologically by a loss of thyroid parenchyma and replacement by adipose connective tissue. It is not known if this form is distinct from the lymphocytic thyroiditis or an end result of thyroiditis.

Causes of acquired secondary hypothyroidism include pituitary malformations and pituitary neoplasia, whereas reported causes of congenital primary hypothyroidism include iodine deficiency, thyroid dysgenesis and dyshormonogenesis.

Incidence and risk factors

The prevalence of canine hypothyroidism is reported to be between 0.2 per cent to 0.8 per cent (Panciera, 1994; Dixon, 1999). Age at the time of diagnosis can vary between 0.5 and 15 years, but hypothyroidism is most commonly diagnosed in middle-aged dogs (four to 10 years old).

It usually affects mid to largesize breeds. Golden retrievers and Dobermann pinschers, as well as Irish setters, miniature schnauzers, Dachshunds and cocker spaniels are among the breeds reported to be at higher risk for hypothyroidism. There is no clear difference in prevalence between male and female dogs.

Clinical signs

Because thyroid hormones influence the function of many organs, hypothyroidism can be in the differential diagnosis of a wide range of problems.

Clinical signs of hypothyroidism may be nonspecific, and hypothyroidism is commonly misdiagnosed. Common clinical signs are attributable to decreased metabolic rate and include lethargy, mental dullness, weight gain, reluctance to exercise and cold intolerance (Panciera, 1994). Obesity occurs in approximately 40 per cent of hypothyroid dogs.

Dermatologic changes occur in 60 per cent to 80 per cent of hypothyroid dogs (Panciera, 1994; Dixon, 1999). Common findings include dry scaly skin, changes in hair coat quality or colour, alopecia, seborrhea and superficial pyoderma (Figure 1). Hyperkeratosis, hyperpigmentation, comedone formation, hypertrichosis, otitis, poor wound healing and, less commonly, myxoedema may also occur. Alopecia is usually bilaterally symmetric and is first evident in the lateral trunk, ventral thorax and tail. Often, the first sign noticed is failure of hair regrowth after clipping.

Hypothyroid dogs are predisposed to recurrent bacterial infections of the skin. Pruritus is usually uncommon, but might occur in cases of concurrent infection. Myxoedema is a rare dermatologic manifestation of hypothyroidism characterised by nonpitting thickening of the skin – especially of the eyelids, cheeks and forehead (Figure 2). This condition can sometimes lead to myxoedema coma, carrying a guarded prognosis.

Other clinical signs include reproductive abnormalities (decreased libido, decreased fertility, cycle abnormalities and abortion), diffuse peripheral neuropathy, cranial nerves deficits, cardiovascular abnormalities (bradycardia, low QRS voltages, inverted T waves) and ocular changes (most commonly corneal lipidosis, corneal ulceration, uveitis).

Laryngeal paralysis and megaoesophagus have been seen with hypothyroidism, but a causal relationship has not been confirmed, and treatment of hypothyroidism does not consistently result in resolution of clinical signs.

Differential diagnosis

The majority of the clinical signs associated with hypothyroidism described above are usually non-specific and the differential diagnosis is extremely broad. In some cases, this situation can lead the clinician to misclassify some signs as hypothyroidism and, consequently, to overlook some other diseases.

Diagnosis

It is important to emphasise the diagnosis of hypothyroidism comprises an agreement between the thyroid function test results and the clinical suspicion of the disease based on a complete history, physical examination and clinicopathological findings.

The indiscriminate use of thyroid function tests alone should be avoided, as it is likely to provide false-positive results. In addition, the identification of a concurrent disease is essential because of their effect on the thyroid function tests (Kantrowitz, 2001).

In hypothyroid patients, the haematology reveals a mild non-regenerative anaemia in 30 per cent of the cases. Hypercholesterolaemia and hypertriglyceridaemia occur in 75 per cent and 88 per cent of cases, respectively. Less common findings are elevated creatine kinase, alkaline phosphatase, glucose or fructosamine levels and decreased phosphorus (Panciera, 1994; Dixon, 1999).

The total thyroxine (tT4) concentration is a good screening test. However, approximately 10 per cent of hypothyroid dogs can be missed if only relying on this test (Table 1). In addition, many drugs and any non-thyroidal illness (NTI) can falsely decrease tT4, resulting in a low specificity (Kantrowitz, 2001). Sight hounds (such as greyhounds or whippets) have a lower tT4 concentration than other breeds.

The total triiodothyronine (tT3) does not usually bring further advantages to the diagnosis of the disease. However, in sight hounds, it remains within normal limits. For this reason, one advantage of performing the tT3 is to support the diagnosis of hypothyroidism in these breeds (Ferguson, 2007).

Free T4 (fT4; measured by equilibrium dialysis) is less affected by NTI and by the presence of anti-T4 antibodies. However, severe non-thyroidal illness can still influence this test, bringing values below the normal limits in some euthyroid dogs (false positive result; Kantrowitz, 2001).

Approximately 25 per cent of hypothyroid dogs have normal TSH values. Elevated TSH is highly suggestive of hypothyroidism, but this can still occur in euthyroid dogs. Possible causes include subclinical hypothyroidism, recovery from NTI, pulsatile secretion of TSH or concurrent drug administration. For this reason, if tT4 or fT4 are within normal limits but TSH is elevated, repeating these tests after four to six weeks is recommended.

In summary, TSH cannot be used to rule out hypothyroidism, but it can confirm hypothyroidism if the tT4 or fT4 are concurrently low (Peterson et al, 1997).

TSH stimulation test

This test relies on evaluating the thyroid functional capacity (low tT4 post-TSH stimulation in hypothyroid patients).

The bovine TSH source is not available, but human TSH is a good alternative and relatively safe to use. This test should be considered when common tests provide equivocal results. The protocol using human TSH is the intravenous administration of 75ìg per dog, with a second blood sample taken after six hours. The diagnosis of hypothyroidism is likely if pre and post-tT4 are below the reference range. In euthyroid dogs, an increase of at least 1.5 times the basal tT4 concentration is expected. However, in some cases, intermediate and, therefore, equivocal results may still occur.

For this test, thyroid supplementation has to be stopped six to eight weeks before (Scott-Moncrieff, 2010).

The thyrotropin-releasing hormone (TRH) stimulation test is less reliable than the TSH stimulation, as some euthyroid patients fail to respond to the test. For this reason, it is not recommended.

Antithyroglobulin antibodies (ATA) can be measured and are a sensitive indicator of thyroiditis, but they are not synonymous with abnormal thyroid function. The presence of ATA may be the earliest indicator of thyroid pathology, but not all dogs with elevated ATA will develop hypothyroidism. In dogs with normal tT4, fT4, TSH but elevated ATA, it is reasonable to monitor the thyroid function every six months. Measurement of ATA is sometimes used for screening breeding dogs of breeds predisposed to the disease.

Thyroid ultrasound can be used to evaluate the thyroid gland volume and echogenicity, but this method is insensitive and depends on the ultrasonographer’s experience.

Scintigraphy using radioactive pertechnetate is the best tool to diagnose hypothyroidism, but it is

expensive, requires anaesthesia and is limited to a few institutions (Scott-Moncrieff, 2010).

The two main factors complicating the diagnosis are concurrent illnesses (NTI) and drug administration. For this reason, it is important to distinguish between NTI and hypothyroidism, and the patient should be evaluated thoroughly.

Many drugs can modify thyroid hormone concentrations (Table 2). The effects of steroids occur mainly at immunosuppressive doses and TSH concentration does not usually change significantly.

Sulphonamides block the iodination of thyroglobulin so they can cause clinical hypothyroidism, but the effects are reversible.

Phenobarbital administration (long term) causes decreased tT4 and fT4 concentrations, whereas administrating potassium bromide does not seem to affect thyroid function significantly at usual dosages (Daminet et al, 2003).

In summary, diagnosis of hypothyroidism might require several tests and possibly repeat measurements over time. In case of clinical suspicion of the disease, we usually start with tT4 together with a canine thyroid-stimulating hormone (cTSH) measurement.

FT4 might be helpful in cases with equivocal results and suspect NTI. In cases where the suspicion of hypothyroidism remains high, but thyroid hormones measurements are normal, a TSH stimulation test could be performed, or tT4/ cTSH levels repeated after four to eight weeks.

Clinical management

The administration of a synthetic form of thyroxine (l-thyroxine) is the mainstay of the treatment. The recommended starting dose is 0.02mg/kg twice a day, and dose adjustment should be done depending on tT4 concentrations and clinical response. A new liquid solution can be administered once daily at 20µg/kg and has been shown to be effective (Le Traon et al, 2009).

Dose monitoring is performed four weeks after initiation of therapy. The goal is to achieve a tT4 concentration at the high end of the normal range, four to six hours postpill (Scott-Moncrieff, 2010). Importantly, the clinical response must be considered as well (for example, if improvement is achieved with a tT4 within the midnormal range, no dose change is necessary). Once clinical signs have improved, once daily dosage can be attempted and, on a long-term basis, tT4 levels should be monitored every four to six months.

It is important to remember that some clinical signs (excessive weight, dermatologic abnormalities) may take several weeks to months to improve or resolve (Figure 3).

Prognosis

Treatment for hypothyroidism is generally life-long and initially needs dose adjustments, but prognosis is excellent.

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