



# Case Report: symptomatic hyperthyroidism associated with carcinoma in a dog

Clara Tullio\*, Stefania Uccheddu

*San Marco Veterinary Clinic (Veggiano, PD, Italy)*

**Abstract:** A mongrel dog, 9-year-old, 22.5 kg neutered female was evaluated for a constant state of anxiety, restlessness and dysorexia. Since she was adopted, at estimated age of 3 years, by a colleague in veterinary medicine she carries out, on her dog, a clinical and neurological examination, and the blood-biochemical and urinary tests, aimed to exclude organics problems, possible causes of the clinical signs arising. The medical investigations carried out were in the normal ranges. It follows that the most probable differential diagnoses are to be referred to behavioral disorders such as: cognitive dysfunction, separation disorders, phobia, anxiety disorders, stereotypies, compulsive disorders. Anyway, also wanting to exclude organic problems, the colleague referred her dog to our clinic for an ultrasound scan. A complete thoraco-abdominal and ventral neck ultrasound examination was performed.

Ultrasound examination of the neck region showed a 3.3 cm by 2.3 cm mass in the right lobe of the thyroid (suspected neoplasm). Subsequently the thyroid profile, which led to a diagnosis of suspected hyperthyroidism a whole-body CT scan (Computed Tomography) confirmed a large right thyroid mass suspected of primary neoplasia. It was decided to proceed surgically with right thyroidectomy, so histological examination confirmed the diagnostic suspicion of thyroid carcinoma.

Following thyroidectomy, the colleague/owner has reported a sudden remission of his behavioral symptoms within a week of its return home. As a follow up, iatrogenic hypothyroidism has resulted, treated with levothyroxine at 0.02 mg/kg BID, with periodic monitoring of hormonal values.

The medical investigation of clinical signs, referable primarily to behavioral disorders, can reveal, in reality, an organic cause, sometimes rare, as in the specific case, both for the diagnostic relief (thyroid cancer and hyperthyroidism) and for the clinical signs associated with it (anxiety, restlessness, disorientation).

*Key Words:* dog, behavior, symptomatic hyperthyroidism.

\* *Corresponding Author:* clara\_ecovet@yahoo.it

## Statement of the Problem

The dog came to the clinic because of anxiety, restlessness and dysorexia for several months at the beginning of the summer and persisting throughout the day, with progressive worsening.

## Signalment

Mixed breed, female, 9 years old, neutered, 22.5 kg weight.

## History

The dog was adopted, already neutered, in a shelter by a veterinary colleague and by her husband, at an estimated age of 3 years.

Immediately after the adoption, the owner reported destruction of objects, vocalizations and restlessness, in the absence of the owners, suggestive of separation disorders (Overall, 1997; Lund & Jorgensen, 1999).

To cope with the problem, the colleague asked for the support of a dog trainer, who enabled her to implement some measures to reduce/eliminate the symptoms through a rehabilitation program.

It was primarily the dog's lack of physical activity that was responsible for what the colleague called 'motivational frustration' as the dog was not routinely stimulated in motor and cognitive pursuits (Takeuchi et al., 2000).

From this point on, the owner gradually began to take longer walks, while at the same time making every effort to take the dog with her to avoid loneliness.

A nutraceutical therapy based on  $\alpha$ -casozepine at 30 mg/kg SID (Horwitz, 2009) had been associated; games and chews were added, with their particular use in the rare moments of the referent's absence and other activities aimed at stimulating the cognitive aspect (Takeuchi et al., 2000).

Improvements occurred very gradually, though without any definitive elimination of separation disorders. However, after a few years and contrary to any expectation, a second adoption took place, to provide solution to the problem: an adult male dog from a rescue kennel. Following a thorough assessment by a behaviorist colleague, the dog was deemed suitable for that household as he was a well-balanced, non-problematic dog.

From that day on, the patient did not show any more disturbances during the absence of the owners, demonstrating a predominantly calm temperament.

The decisive therapeutic effect, given by the arrival of the new cohabiting dog, could be traced back to that aspect of social influence, as social support, able to reduce fear and anxiety in an individual, thanks to the mere presence of a conspecific (Ferraris, 2013), allowing for the maintenance of homeostasis even in the absence of the owners.

After the resolution of the issue (few years later) a second problem arose. At the beginning of the summer, when the dog was 9 years old, the owner reported a new behavioral issue.

The colleague reported that her dog was in a constant state of agitation, day and night, pointing out that the patient used with the following statements: 'she is panting a lot, she is constantly changing position and repeatedly moving from one kennel to another, she is disorientated, wanders aimlessly, often vocalizes simulating a sort of lament, her appetite has become capricious and selective. Moreover, she often tries to escape, sometimes succeeding, ... we are worried and there is not enough silence to sleep; all this even during a holiday period at the seaside, with us, all together.'

The patient was referred to our facility for an ultrasound scan, after a clinical and neurological examination, all of which resulted in normalcy. The scan was aimed to exclude organic problems, responsible for the recent behavioral changes. Considering that, shortly before the onset of symptoms, the blood-biochemical and urinary tests, performed as routine annual monitoring, were within normal ranges.

## Physical Examination Findings and Laboratory Results

At the clinical examination, no significant changes were noted (temperature, pulse and breathing were normal) with a Body Condition Score of 4 on a scale of 5 (overweight).

A complete thoraco-abdominal and ventral neck ultrasound examination was performed; and as already reported, aimed to exclude organics problems.

The thoraco-abdominal ultrasound examination showed mild focal lesions in the spleen and sporadic renal cortical mineralization.

Echocardiography showed a small persistent ductus arteriosus, without signs of remodeling and hemodynamically insignificant.

Ultrasound examination of the neck region showed a 3.3 cm by 2.3 cm mass in the right lobe of the thyroid, richly vascularized with focal areas of calcification (suspected neoplasm).

In-depth level II diagnostics were recommended after repetitions of blood tests including thyroid function parameters.

The haemato-biochemical and urinary tests were within normal ranges, apart from the thyroid profile, which led to a diagnosis of suspected hyperthyroidism (Table 1).

**Table 1.** Thyroid profile.

Thyroid profile	Result	Reference range (minimum value)	Reference range (maximum value)
TSH (ng/ml)	0.03	0.03	0.4
4TT4 (µg/dl)	5.41	1	3.5
fT4 (pmol/l)	74.4	15.1	42.3
FT4 LC-MS-MS (pmol/l)	65.9	12.8	47.3
FT3 LC-MS-MS (pmol/l)	3.32	1.41	5.34
RFT3 LC-MS-MS (pmol/l)	2.94	1.23	5.13
FT3/rFT	1.13	0.69	2.03

CT (computed tomography) examination was then performed for further characterization of the thyroid lesion and staging the patient.

Whole-body CT scan confirmed a large right thyroid mass suspected of primary neoplasia. In the abdomen, multiple peritoneal nodules were disclosed of nature to be determined (histopathological sampling was recommended) and multiple focal area in the splenic parenchyma, consistent with extramedullary hematopoiesis.

Thoracic scan showed a vascular anomaly due to persistent aorto-pulmonary connection via ductus arteriosus and rare pulmonary mineralized micronodules (probably dystrophic).

The brain was normal.

## Diagnosis

Based on the patient's clinical manifestations, the differential diagnoses related more to the following behavioral disorders.

Cognitive syndrome of the elderly dog, phobias, separation disorders, permanent generalized anxiety, hypersensitivity / hyperactivity, stereotypies, compulsive disorders (Landsberg et al., 2013; Siracusa, 2017).

Organic neurological disorders, sensory deficits, endocrine, metabolic and musculoskeletal disorders with a predominantly algic component are not excluded.

Cases of secreting thyroid neoplasia are rare in dogs (Bezzola, 2002) and therefore more unlikely to be included among differential diagnoses.

In fact, sporadic cases have been described in the literature, with symptoms mostly related to the mechanical compression created by the mass, such as cough and dysphagia, sometimes wheezing, polyuria/polydipsia, with behavioral changes generally not very evident (Abbott, 2000; Liptak, 2007; Wucherer et al., 2010; Campos et al., 2012).

Differently from dogs, as a comparison of species, adult cats commonly have thyroid-secreting adenomas that in 70% of cases affect both lobes (Labuc & Jones, 1988; Meric, 1989; Broussard et al., 1995) and the related symptoms are more specific and evident. This is the case with instances of weight loss, polyphagia, gastrointestinal disorders: vomiting, diarrhea, increase in fecal volume (Holzworth et al., 1980; Broussard et al., 1995).

Hyperactivity, irritability, sometimes puppy-like attitudes due to greater motivation to play (wrongly interpreted by the owners as a state of well-being), anxiety, vocalizations, ventroflexion of the neck due to muscular atrophy and weakness, ataxia and aggressiveness, overgrooming with traumatic alopecia of the stomach and sometimes of the flank. Thus, symptoms that can also be referred to as behavioral problems (Nemzecz et al., 1994; Vogelnest, 2017; Miller et al., 2019).

In humans, thyroid nodular diseases are frequent but malignant forms are rare (Wémeau, 2009),

even with thyroid carcinoma gradually increasing worldwide (Cabanillas et al., 2016).

Moreover, in the case of hyperthyroidism symptoms differ between young and old, being more specific in young people, who present sweating, tremors, slimming, exophthalmos and non-specific in the elderly, resulting in atrial fibrillation and heart failure (Pasqualetti et al., 2017).

With reference to our patient, based on all the investigations performed, to ensure a diagnosis of certainty, we first proceeded with cytopathological examination of the thyroid lesion, the result of which primarily defined the presence of a thyroid carcinoma. Second, the cytopathology of the peritoneal nodules suggests mesothelial reactivity.

## Treatment

It was decided to proceed surgically with right thyroidectomy, after isolation of the recurrent laryngeal nerve and closure of the vessels with hemoclip.

A laparoscopy was also performed to investigate the peritoneal lesions, brownish nodular in appearance and biopsied with oval grasping forceps.

Subsequent histological examination confirmed the diagnostic suspicion of thyroid carcinoma and the reactive nature of the peritoneal lesions.

## Follow-up

The patient remained in hospital for a few days, showing a stable clinical situation.

After his discharge he was followed by the colleague/owner, who reported a sudden remission of his behavioral symptoms within a week of his return home.

In fact, the dog no longer showed restlessness, anxiety, vocalizations and wandering aimlessly. It also resumed eating normally (twice a day with home-made food) and went back to living his daily routine, leading to a return to well-being for the whole family.

Although the histopathology report pointed out a tumoral vascular invasion, the dog experienced an unexpectedly long remission (Campos et al., 2014) and to date, five years after recovery, the patient has not presented any organic or behavioral problems, with the exception of a iatrogenic hypothyroidism, treated with levothyroxine at 0.02 mg/kg BID (Nachereir et al., 1993), with periodic monitoring of hormonal values.

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## Case Report: ipertiroidismo sintomatico associato con carcinoma in un cane

Clara Tullio, Stefania Uccheddu

*San Marco Veterinary Clinic (Veggiano, PD, Italy)*

### *Sintesi*

Un cane meticcio femmina di 9 anni, 22,5 kg, sterilizzata, è stata esaminata per stato d'ansia permanente, irrequietezza e disoressia. Poiché adottata ad un'età stimata di 3 anni, da una collega, Medico Veterinario, essa stessa esegue, sul proprio cane, una visita clinica e neurologica e gli esami del sangue, al fine di valutare possibili cause dei segni clinici insorti, non rilevando a riguardo alterazioni. Ne consegue che le diagnosi differenziali più probabili, al momento, siano da riferire a disturbi comportamentali quali: sindrome cognitiva del cane anziano, fobie, disturbi da separazione, problematiche d'ansia, stereotipie, disturbi compulsivi. Ad ogni modo, volendo escludere anche cause organiche, la collega richiede un'ulteriore indagine ultrasonografica completa, di referenza, presso la clinica veterinaria per cui lavoriamo.

L'esame ecografico effettuato comprende addome, torace e regione ventrale del collo, da cui emerge la presenza di una massa a livello di lobo tiroideo destro, riferibile primariamente a neoplasia. Il sospetto viene confermato dalla citopatologia. Si opta per un profilo tiroideo con valori indicativi di ipertiroidismo ed una CT (Computed Tomography) con esito sovrapponibile alle indagini ultrasonografiche. Si decide di effettuare una tiroidectomia destra con esame istopatologico della lesione che attesta la presenza di un carcinoma tiroideo.

A seguito dell'intervento la collega riporta una repentina risoluzione dei segni clinici, nell'arco di una settimana dalle dimissioni. Il follow up indica l'insorgenza di un ipotiroidismo iatrogeno, trattato con levotiroxina a 0,02 mg/kg BID con monitoraggio periodico dei valori ormonali.

L'indagine accurata dei segni clinici, riferibili primariamente a disturbi comportamentali, può far emergere in realtà una causa organica, talvolta rara, come in questo caso specifico, sia per il rilievo diagnostico (carcinoma tiroideo secernente), sia per i segni clinici ad esso associati (ansia, irrequietezza, disorientamento, disoressia).

