CASE REPORT

Hyperthyroidism due to an intrathoracic tumour in a dog with test results suggesting hyperadrenocorticism

The elevated urinary corticoid/creatinine ratios of an 11-year-old Jack Russell terrier with polyuria were suppressible in a high-dose dexamethasone suppression test, which was suggestive of pituitary-dependent hyperadrenocorticism. The absence of physical and routine-laboratory changes compatible with hyperadrenocorticism and the relatively high plasma thyroxine concentration were the impetus for additional studies of thyroid and adrenocortical functions. A high plasma thyroxine concentration (62 nmol/l; 5·0 μg/100 ml) suggested the presence of hyperthyroidism. Radiography, $^{99m}TcO_4^-$ scintigraphy, ultrasonography, computed tomography and cytology revealed a hyperfunctioning intrathoracic thyroid tumour. In the low-dose dexamethasone suppression test, the plasma cortisol concentration exceeded the reference value of 40 nmol/l (1·4 μg/100 ml) at eight hours after dexamethasone administration (0·01 mg/kg intravenously), a test result compatible with hyperadrenocorticism. In conclusion, this report represents the first case of a dog with an autonomously hyperfunctioning thyroid tumour in the thorax. The elevated urinary corticoid excretion and the positive low-dose dexamethasone suppression test may be explained by alterations in cortisol metabolism, the stress of the hyperthyroid state or both.

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INTRODUCTION

Syndromes of hormone excess or deficiency often affect other endocrine systems. For example, in dogs, glucocorticoid excess leads to low plasma concentrations of thyroxine (T_4) and tri-iodothyronine (Kemppainen and others 1983). Glucocorticoids affect a variety of aspects of thyroid hormone secretion and metabolism, such as the production or clearance of T_4, peripheral conversion of T_4, renal clearance of iodide and the production or clearance of circulating thyroid-hormone-binding protein (Kaptein and others 1992, Dluhy 2000).

Conversely, from studies in experimental animals and in human beings, it is known that an excess of thyroid hormone causes accelerated cortisol clearance as well as changes in the pathways of cortisol degradation (Dluhy 2000). In cats with spontaneous hyperthyroidism due to thyroid adenomas, elevated urinary corticoid: creatinine ratios (UCCRs) have been reported. This has been ascribed to increased cortisol clearance and activation of the pituitary-adrenocortical axis (de Lange and others 2004).

Hyperthyroidism is rare in dogs. Thyroid tumours are often malignant, and in only 10 to 20 per cent of cases is there hypersecretion of thyroid hormone (Leav and others 1976, Mooney 2005). These tumours usually originate from eutopic thyroid glands, but they may also arise from ectopic thyroid tissue. About 50 per cent of healthy dogs have ectopic thyroid tissue (Godwin 1936, Blessing and Zaborsky 1966, Kameda 1972), as a result of thyroid tissue remaining at the level of the thyroglossal duct and/or descending with the heart during embryonic development.

Until now, there have been no reports on the adrenocortical function of dogs with hyperthyroidism. This case study reports on a polyuric dog with an ectopic hyperfunctioning thyroid tumour, with results of adrenocortical function studies that initially suggested the presence of pituitary-dependent hyperadrenocorticism.

CASE HISTORY

An 11-year-old, male neutered Jack Russell terrier, weighing 8 kg, was examined by the local veterinarian for gradually worsening polyuria and polydipsia. The increased water intake had been noticed for the first time a few months earlier but had been ascribed to a change of diet.

At that time, the dog was in good condition and physical examination had not revealed any abnormalities. Results of blood chemistry, haematology and urinalysis were unremarkable, except for a low specific urine gravity.

The plasma T_4 concentration (45 nmol/l; 3·5 μg/100 ml) approached the upper limit of the reference range (19 to 46 mmol/l; 1·5 to 3·6 μg/100 ml). The basal UCCR, measured in two urine samples collected on two consecutive mornings (20×10^{-6} and 14×10^{-6}), exceeded the range found in 89 healthy dogs (0·3 to $8{\cdot}3\times10^{-6}$; Van Vonderen and others 1997). Following the administration of three oral doses of 1 mg dexamethasone at eight hour intervals, the UCCR had decreased to $4{\cdot}2\times10^{-6}$. These findings were compatible with pituitary-dependent hyperadrenocorticism. However, there was some concern about this diagnosis because the dog had no physical signs of the disease and none of the usual biochemical changes, such as low T_4 and elevated alkaline phosphatase (Teske and others 1989). The dog was referred to the Utrecht University Clinic for Companion Animals, the Netherlands.

At the time of admission, the polyuria had existed for about six months. The dog was still in good condition. Its appetite was good and there was no weight loss. The owner had noticed that the dog preferred cool places to lie down and panted frequently. The owner reported seeing abdominal distension only before micturition. The hair coat was unchanged, but there was less shedding. On physical examination, the pulse rate was high (160 bpm). In the neck area, no thyroid enlargement could be palpated.

Laboratory investigations revealed that the plasma concentration of alkaline phosphatase (26 U/l) was still within the reference range (<73 U/l). The basal UCCR had increased further (33×10^{-6} and 19×10^{-6}). The elevated plasma T_4 concentration (62 nmol/l) and the low plasma thyroid-stimulating hormone (TSH) concentration (<0·02 μg/l; reference <0·60 μg/l) were compatible with hyperthyroidism. It was assumed that the hyperthyroidism was due to an intrathoracic thyroid tumour, and that the elevated UCCR was secondary to the hyperthyroid state. Additional investigations were performed to test this hypothesis.

Scintiscanning after intravenous administration of 7·5 MBq (0·2 mCi) $^{99m}TcO_4^-$ revealed uptake not only in areas of physiological iodide uptake, such as the parotid salivary gland and the gastric mucosa, but also in the cranial part of the thorax. There was almost no uptake by the thyroid glands (Fig 1). Thoracic radiographs visualised a large mass in the cranial mediastinum (Fig 2). On ultrasonography, the mass had mixed echogenicity with several small cysts. Cytological examination of ultrasound-guided fine-needle biopsies revealed epithelial glandular tissue, compatible with thyroid tumour tissue (Fig 3). On contrast-enhanced computed tomography (CT), the mass was well circumscribed without signs of blood vessel invasion (Fig 4). There was no evidence of pulmonary metastases other than one very small nodule in the periphery of the right cranial lung lobe.

An intravenous low-dose dexamethasone suppression test (LDDST) was performed with blood collection for cortisol and adrenocorticotrophic hormone (ACTH) measurements at −15 minutes, immediately before and two, four, six and eight hours after intravenous administration of 0·01 mg/kg dexamethasone (Rijnberk and others 2001). As with the plasma ACTH concentration, the plasma cortisol concentration decreased to 10 nmol/l (0·4 μg/100 ml) four hours after dexamethasone administration. At eight hours, the plasma cortisol concentration (44 nmol/l; 1·6 μg/100 ml) exceeded the reference value of 40 nmol/l (1·4 μg/100 ml) (Fig 5). On contrast-enhanced CT, the pituitary gland was uniformly enhanced and not enlarged.

The owner declined the proposed surgical treatment, and the dog was euthanased two months later without postmortem examination.

DISCUSSION

There are several case reports of dogs with tumours originating from ectopic thyroid tissue in the thorax (Stephens and others 1982, Walsh and Diters 1984, Ware and others 1994, Constantino-Casas and others 1996). Ectopic thyroid tumours may also occur cranial to the thyroid gland. These tumours arise from thyroglossal duct remnants (Harkema and others 1984, Lantz & Salisbury 1989) and may involve the base of the tongue. Similar to eutopic tumours, ectopic tumours often have malignant features (Leav and others 1976). The neoplastic transformation may be associated with (partially) defective thyroid hormone synthesis, leading to the release of iodinated albumin (Leav and others 1976, Rijnberk 1996).

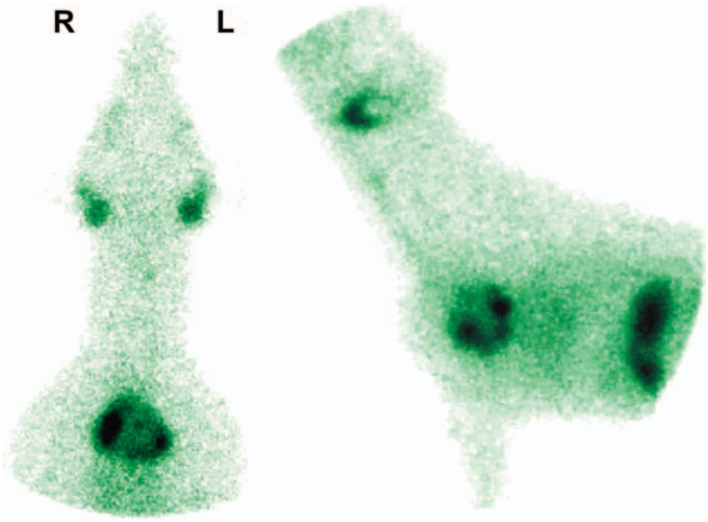

FIG 1. Scintiscan made 45 minutes after intravenous injection of $^{99m}TcO_4^-$. There is normal distribution of radioactivity in the salivary glands and gastric mucosa, but almost none in the thyroid glands. An increased uptake is seen in the cranial part of the thorax

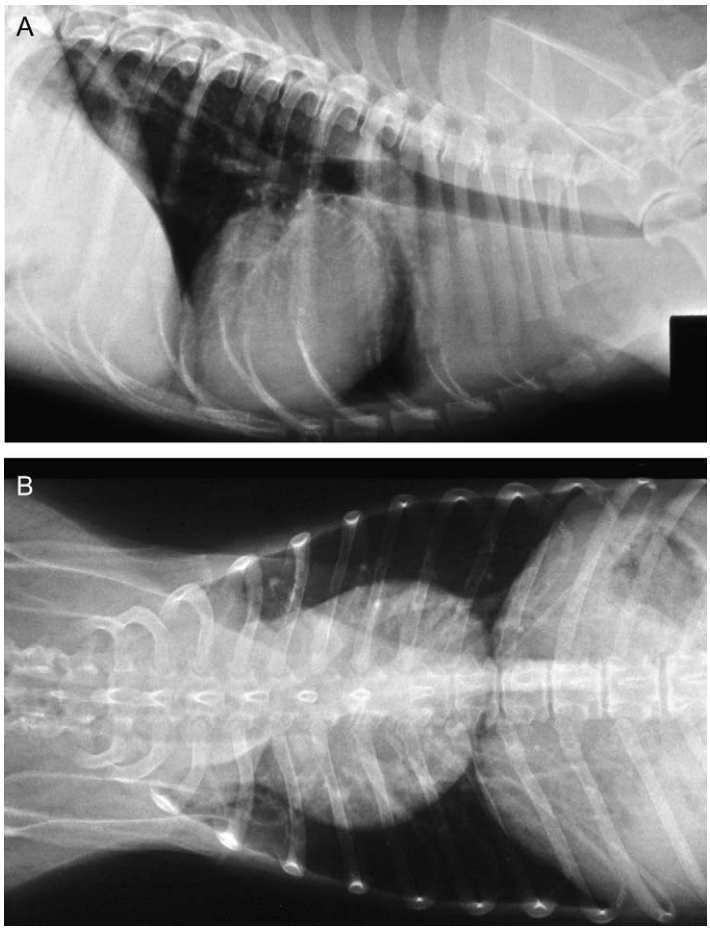

FIG 2. Lateral (A) and dorsoventral (B) radiographs of the thorax showing a mass in the cranial mediastinum

Like eutopic tumours, ectopic tumours may also secrete excessive amounts of thyroid hormones. To date, there is only one report of a dog with hyperthyroidism due to an ectopic tumour. This tumour was located in the ventral portion of the pharyngeal wall at the base of the tongue (Rijnberk 1981). Here, we report on an intrathoracic thyroid tumour causing hyperthyroidism. The autonomous and excessive thyroid hormone secretion suppressed the release of TSH, which led to almost no $^{99m}TcO_4^-$ uptake in the eutopic thyroid tissue.

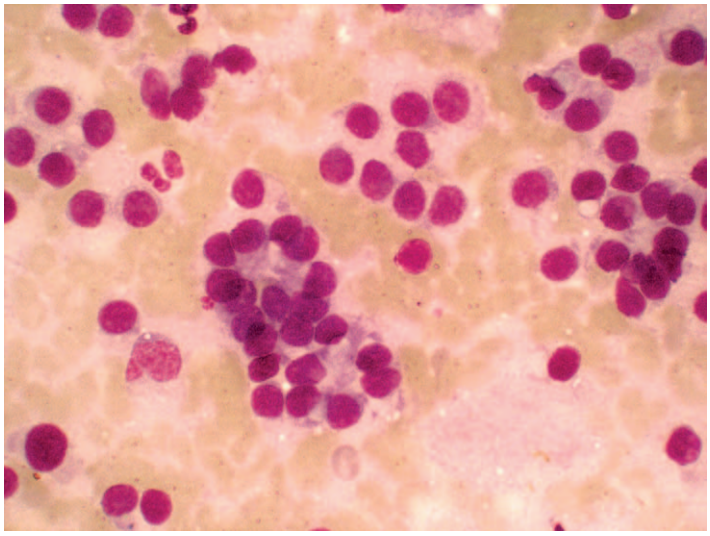

FIG 3. Cytology of a fine-needle biopsy of the thoracic mass with acinar arrangement of epithelial cells with a moderate amount of cytoplasm. May-Grünwald-Giemsa. ×500

In this dog, the hyperthyroidism was associated with biochemical changes compatible with hyperadrenocorticism, that is, elevated UCCRs and positive LDDST. However, there were no physical or routine laboratory data suggesting hyperadrenocorticism. Also the diagnostic imaging of the pituitary gland did not reveal any changes. In the absence of indications for co-existent hyperadrenocorticism, other explanations for these findings were explored, which will be discussed in the order of (i) increased UCCRs and (ii) positive LDDST.

The increased UCCRs might be due to an increase in the rate of metabolic breakdown and transformation of cortisol. This has been documented in human beings and more recently in cats (Gallagher and others 1972, Linquette and others 1975, Larsen and Ingbar 1992, Dluhy 2000, de Lange and others 2004).

The rapid disposal of cortisol and its increased transformation into inactive metabolites that are unable to suppress the hypothalamus-pituitary system results in an increased pituitary release of ACTH and consequently increased cortisol secretion (Gallagher and others 1972). Thus, despite an enhanced breakdown and conversion of cortisol, plasma cortisol levels remain normal. The combination of increased breakdown/transformation and increased cortisol production results in elevated urinary concentrations of cortisol and cortisol metabolites (Hellman and others 1961, Dhuly 2000).

In the LDDST, the plasma cortisol concentration at eight hours after dexamethasone administration exceeded the reference value of 40 nmol/l (1·4 µg/100 ml) (Rijnberk and Mol 1997, Feldman and Nelson 2004). In principle, this abnormal test result may be a reflection of stress of disease, as has been previously suggested (Chastain and others 1986; Kaplan and others 1995; Gieger and others 2003). Another explanation,

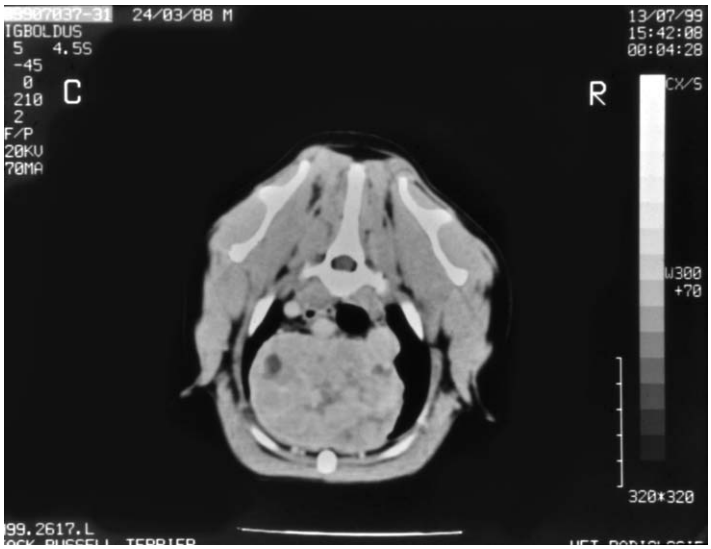

FIG 4. Contrast-enhanced computed tomography image of the cranial part of the thorax. The tumour is well circumscribed and there are no indications of invasion of blood vessels. The small radiolucent areas are cysts

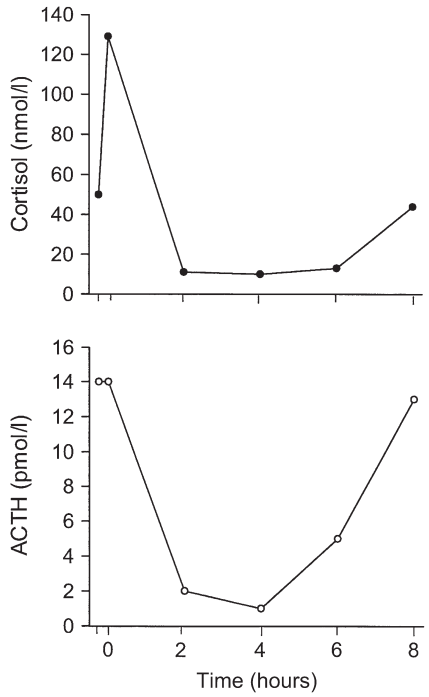

FIG 5. Plasma cortisol and adrenocorticotrophic hormone (ACTH) concentrations before and after intravenous administration (at time point 0) of 0·01 mg/kg dexamethasone

fitting in with the explanation of the elevated UCCRs, could be that the high cortisol concentrations at six and eight hours were the result of an escape from suppression, due to the above discussed increased clearance of glucocorticoids (including dexamethasone). A similar mechanism has been reported in dogs with hyperadrenocorticism (Lothrop and Oliver 1984).

Conclusions

This report represents the first case of a dog with an autonomously hyperfunctioning thyroid tumour in the thorax. The elevated corticoid excretion and the escape in the LDDST may be explained as being a consequence of hyperthyroidism-induced alterations in the metabolism and excretion of cortisol.

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