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Review

Endocrine tumours in the guinea pig

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ABSTRACT

Functional endocrine tumours have long been thought to be rare in guinea pigs, although conditions such as hyperthyroidism and hyperadrenocorticism have been documented with increasing frequency so the prevalence of hormonal disorders may have been underestimated. Both the clinical signs and diagnosis of hyperthyroidism in guinea pigs appear to be very similar to those described in feline hyperthyroidism, and methimazole has been proven to be a practical therapy option. Hyperadrenocorticism has been confirmed in several guinea pigs with an adrenocorticotropic hormone stimulation test using saliva as a non-invasive sample matrix; trilostane has been successfully used to treat a guinea pig with hyperadrenocorticism. Insulinomas have only rarely been documented in guinea pigs and one animal was effectively treated with diazoxide.

Introduction

Until recently, endocrine tumours were reported to occur very rarely in guinea pigs and only endocrine disorders such as functional ovarian cysts have been comprehensively described in this species (Keller et al., 1987; Beregi et al., 1999; Shi et al., 2002; Nielsen et al., 2003). However, over the last decade, neoplasms with endocrine activity, such as thyroid tumours, adrenal gland tumours, and beta-cell tumours have been reported in guinea pigs with increasing frequency (Gaschen et al., 1998; Vannevel and Wilcock, 2005; Gibbons et al., 2013). Endocrine tumours in guinea pigs may be underdiagnosed due to a lack of practical information on diagnostic procedures for these conditions (Zeugswetter et al., 2007; Mayer et al., 2010; Künzel et al., 2013; Ohlhafer, 2013).

Hyperthyroidism

Prevalence of thyroid tumours in guinea pigs may have been underestimated. In a recently conducted survey, thyroid neoplasms were detected in 3.6% (19/236) of the cases that were submitted to a pathological unit in the USA (Gibbons et al., 2013). Contrary to cats, in which thyroid masses are almost always benign, adenocarcinomas have been diagnosed in 36.8% (Gibbons et al., 2013) and 55.5% (Hierlmeier, 2009) of guinea pigs with thyroid tumours, although metastasis has only rarely been reported (Hierlmeier, 2009; Gibbons et al., 2013). Thyroid tumours may be associated with hyperthyroidism, but they have also been reported as non-functional in guinea pigs (Zarrin, 1974; LaRegina and Wightman, 1979; Mayer et al., 2009; Ohlhafer, 2013; Pignon and Mayer, 2013). Currently, the underlying cause of hyperthyroidism in guinea pigs is unclear.

Unlike for cats, the current literature includes only limited information regarding spontaneous hyperthyroidism in guinea pigs, much of which has been documented in case reports and reviews (Mayer et al., 2010; Brandão et al., 2013; Pignon and Mayer, 2013). There are only two case series reporting clinical signs, diagnosis, treatment and outcome of guinea pigs with hyperthyroidism (Künzel et al., 2013; Ohlhafer, 2013). The lack of knowledge regarding the existence of hyperthyroidism in guinea pigs and lack of familiarity of veterinarians with diagnostic testing in this species may lead to an underdiagnosis of hyperthyroidism (Brandão et al., 2013).

According to Künzel et al. (2013), hyperthyroidism was diagnosed in 1.3% (4/309) of the guinea pigs presented to the Clinic for Small Animals of the University of Veterinary Medicine Vienna over a 2.5-year period. Consistent with feline hyperthyroidism, functional thyroid tumours are commonly diagnosed in middle-aged to older (>3 years) guinea pigs (Mayer et al., 2009; Künzel et al., 2013; Ohlhafer, 2013). Sex predisposition has not yet been reported.

Clinical signs

Clinical signs consistent with functional thyroid gland tumours in guinea pigs are very similar to those observed in feline hyperthyroidism and commonly include weight loss (despite normal or increased appetite), a mass in the ventral neck, and behavioural abnormalities in terms of hyperactivity (LaRegina and Wightman, 1979; Thoday and Mooney, 1992; Broussard et al., 1995; Mayer et al., 2009, 2010; Künzel et al., 2013; Ohlhafer, 2013; Pignon and Mayer, 2013) (Figs. 1a, b). However, especially in the early stages of the disease,

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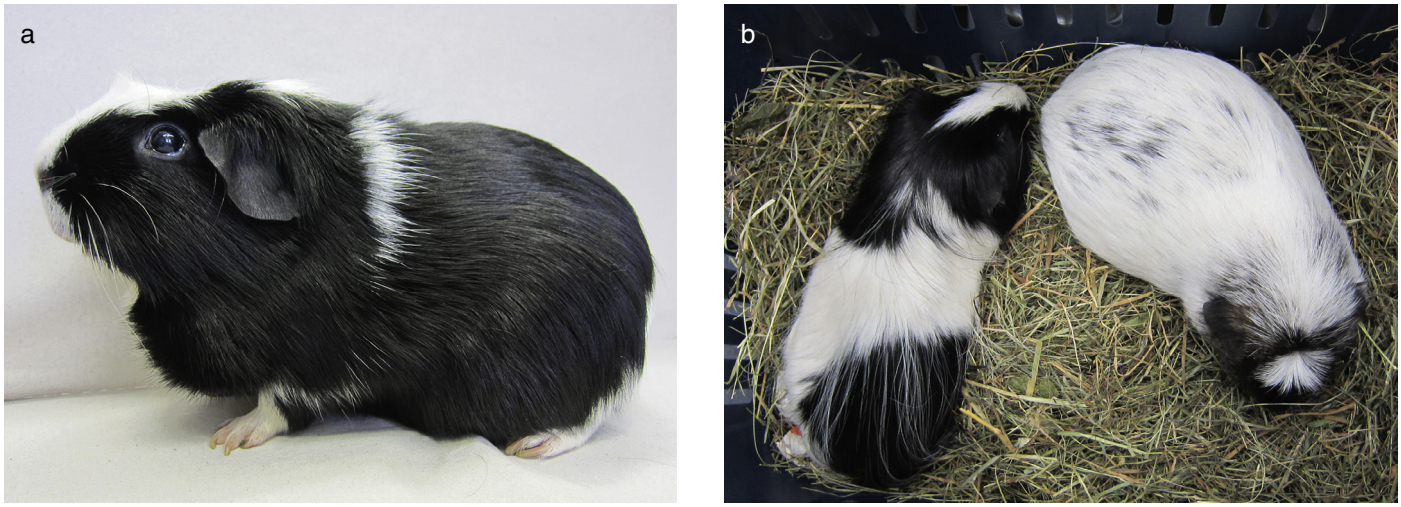

Fig. 1. (a) Hyperthyroidal guinea pig with a visible mass on the ventral neck. (b) Guinea pig with confirmed hyperthyroidism and a healthy companion animal. Note the poor body condition of the hyperthyroidal guinea pig.

clinical signs may be insidious and owners often assume that the signs are the normal result of aging. In addition to hyperactivity and restlessness, behavioural abnormalities may include signs such as prolonged sleeping periods accompanied with difficulties to arouse from sleep, and segregation from the other animals of the social group (Künzel et al., 2013; Ohlhafer, 2013). Other typical signs may include polyuria/polydipsia, tachycardia, tachypnoea, and intensified arterial pulses (Goodkind, 1968; Mayer et al., 2009; Künzel et al., 2013; Ohlhafer, 2013). Some animals are reported to have a matted, ill-kempt, or greasy hair-coat as has been documented in cats with hyperthyroidism (Thoday and Mooney, 1992; Broussard et al., 1995; Künzel et al., 2013). Although, soft stools and alopecia have been anecdotally reported to occur, these signs have never been confirmed in guinea pigs with documented hyperthyroidism (Künzel et al., 2013; Ohlhafer, 2013; Pignon and Mayer, 2013).

Diagnostic work-up

In the case of thyroid gland tumours, sonography commonly reveals a non-homogeneous, cystic mass (Künzel et al., 2013). In principle, fine needle aspiration with cytological evaluation of the mass in the ventral neck could aid in determining of the type of the tumour, and might allow differentiation from other relevant swellings such as cervical lymphadenitis, abscesses, and lymphoma (Brandão et al., 2013). However, puncture of the mass may lead to severe bleeding and should be performed with caution (Künzel et al., 2013; Ohlhafer, 2013). Moreover, similar to humans, cytology does not allow distinction between benign and malignant thyroid gland tumours (Lundgren et al., 2008). If there is cystic pathology of the thyroid gland, the fluid can be aspirated and analysed for thyroid hormones.

As with cats, a definitive diagnosis of hyperthyroidism in guinea pigs is often enabled by the determination of serum total T4 concentrations (Künzel et al., 2013; Peterson, 2013; Zimmerman et al., 2015). Reference intervals for circulating thyroxin concentrations (14.2–64.4 nmol/L for females and 14.2–57.9 nmol/L for males) have recently been published for healthy guinea pigs using a competitive chemiluminescence immunoassay (Müller et al., 2009). The test has become the preferred assay for the determination of total T4 concentrations in cats by many laboratories because it is automated and no radioactive reagents are needed (Peterson, 2013).

In other species, measurement of circulating total thyroxin concentrations can be problematic due to daily variations in the hormone concentration, the presence of concurrent systemic diseases and exogenous factors (Peterson et al., 1990). Therefore, it is possible for guinea pigs with hyperthyroidism to have lower circulating total T4 concentrations, hiding a possible hyperthyroid condition (Mayer et al., 2009). In cases of an early or mild hyperthyroidism, definitive diagnosis may be difficult to achieve and in cases of suspected hyperthyroidism where circulating T4 concentrations are within the normal reference interval, repetitive determinations of total thyroxin concentrations should be undertaken every few weeks (Peterson et al., 1990). In addition, determination of serum concentration of free T4 may be an alternative method for confirming hyperthyroidism (Mayer et al., 2009). The use recombinant human thyroid-stimulating hormone (rhTSH) for a TSH response test has been demonstrated in healthy guinea pigs. However, further studies are needed in order to evaluate the appropriate dose of rhTSH and the optimal point of time for sampling post-TSH in hyperthyroid guinea pigs and non-thyroidal illnesses (Mayer et al., 2013).

Besides total T4 concentrations, blood analysis should always include a biochemical profile (glucose, urea, creatinine, alanine transaminase [ALT], and glutamate dehydrogenase [GLDH]). In cats and humans with hyperthyroidism, liver enzymes (ALT and alkaline phosphatase [ALP]) are almost always increased (Shiel and Mooney, 2007; Kubota et al., 2008). According to one study, in hyperthyroid guinea pigs only ALT was mildly increased, whereas glutamate dehydrogenase (GLDH) was within the reference interval in all cases (Künzel et al., 2013).

Thoracic radiographs may be indicated to identify metastatic neoplasia, although, until now, only two cases with lung metastasis have been reported in guinea pigs with a thyroid carcinoma (Hierlmeier, 2009; Gibbons et al., 2013).

Hypertension, which is diagnosed in approximately 15% of hyperthyroid cats, is known to be a reason for a decreased survival time (Peterson et al., 1983; Thoday and Mooney, 1992). However, measuring the blood pressure is difficult to perform in guinea pigs and therefore not part of routine examination. The consequences of systemic hypertension (like hypertensive retinopathy and ocular haemorrhage) that have been observed in cats have not been documented in guinea pigs (Stiles et al., 1994).

Scintigraphy, which is considered the modality of choice within imaging methods in the diagnosis of feline hyperthyroidism, has been successfully performed in guinea pigs with a functional active thyroid gland (Mayer et al., 2009) (Figs. 2a, b). However, thyroid scintigraphy as a routine method for diagnosis of hyperthyroidism in guinea