Abstract

Hyperthyroidism is arguably the most frequently diagnosed endocrine disorder in cats, with multisystemic manifestations due to the overproduction of the thyroid hormones thyroxine (T4) and triiodothyronine (T3) by a hyperplastic thyroid gland. This can be due to unilateral (30%) or bilateral (70%) functional adenomatous thyroid lobe hyperplasia. Thyroid carcinoma is rare, accounting for < 2% of hyperthyroid cases. Cats older than 8 years (mean age 12-13 years) of any sex are usually affected. Siamese and Himalayan breeds are at decreased risk. Risk factors such as the consumption of tinned cat food, (especially fish or liver and giblet flavour) and the use of cat litter have been identified. The disease has a worldwide distribution, but a very variable incidence - for instance, a low incidence in South Africa and Hong Kong and a high incidence in the UK and USA [1].

Historical and physical examination findings

The thyroid gland was first described by Vesalius in the 16th century. It was later named from the Greek word, thyreos, or shield, based on its physical appearance. The disease was first described in humans in 1913 and in cats in 1979 [2]. The number and severity of clinical signs will vary, depending on the duration of the condition and the presence of concomitant abnormalities in other organs. They are listed in decreasing order of importance [3].

- Weight loss, despite vigorous appetite.
- Signs of increased irritability such as hyperactivity, aggression, abbreviated sleep and restlessness.
- Vomiting occurs in up to 30% of cases due to dysregulation of bowel movements and the increased speed of food consumption.
- Many cats have diarrhoea and increased faecal volume.
- Pu/pd may occur in up to 50% of cats.

These patients usually resist physical examination and are uncharacteristically aggressive, yet can be extremely fragile and can collapse and even die if undue restraint is employed. They usually have a thin body
condition. Thyroid gland enlargement is palpable in 90% of cases. Many cases have tachycardia and heart murmurs due to a concomitant hypertrophic cardiomyopathy, whereas tachypnoea, panting and dyspnoea is seen in many cases. In a small percentage (about 10%) of cases, hyperactivity is replaced by depression and polyphagia by anorexia. – this is termed “apathetic hyperthyroidism” and occurs in advanced cases or cases with severe concomitant disease such as congestive heart failure or neoplasia. Ophthalmoscopic examination can reveal evidence of hypertension (usually if concomitant renal disease is present) with retinal vessel engorgement and rarely retinal detachment. An unkempt and matted coat, presumably due to undergrooming, is often present. Learn to palpate the thyroid glands of all cats coming in for annual vaccinations. Hold the neck in moderate extension and slide thumb and forefinger down either side of the trachea from the larynx down to the thoracic inlet. The two glands can be felt as little blips passing underneath the fingers in the mid-cervical region. Sometimes the enlarged thyroid glands can descend into the thoracic cavity and become impalpable. Be warned that chronic vomition can be a sign of hyperthyroidism.

**Aetiology and Pathophysiology**

Adenomatous (benign) enlargement of thyroid tissue leads to excessive production of thyroxine (T4) and T3, however, the aetiology of this condition is currently unknown. Epidemiological studies have shown an increased risk for cats consuming tinned cat food. It is uncertain whether these cats are just the ones receiving better care, thereby getting older and therefore have a greater chance of developing hyperthyroidism. Although commercial cat food contains large amounts of iodine, studies have failed to demonstrate a correlation between dietary iodine and feline hyperthyroidism. By and large, several goitrogenic substances are commonly found in the environment and in cat food, most notably substances such as phthalates, resorcinol, polyphenols and polychlorinated biphenyls. Most of these hydrocarbons are metabolized via glucuronidation, a process that is unusually slow in cats [4]. Down-regulation of TSH receptor G proteins has been implicated as a pathomechanism in this disease [5].

**Diagnosis**

Differential diagnoses for important clinical signs seen in hyperthyroidism, are the following:

**Weight loss**

- Neoplasia, esp. intestinal
- Diabetes mellitus
- Inflammatory bowel disease
- Glomerulonephritis/chronic kidney disease

**Vomiting**

- Inflammatory bowel disease
- Intestinal lymphoma
- Intestinal foreign bodies
- Chronic pancreatitis
- Cholangiohepatitis
PU/PD

- Diabetes mellitus
- Chronic kidney disease
- Hepatopathy
- Hypercalcaemia
- Hyperadrenocorticism

Minimum database

Haematology – Increased haematocrit in seen in 40 – 50% of cases and some might show a stress leukogram.

Serum Biochemistry - Increased Alt and Alp is found in more than 75% of cases - these can be very early changes and should prompt further investigation. They usually return to values within the reference range with successful therapy [6]. Hyperphosphataemia is seen in up to 20% of cases nowadays, decreasing from its previous prevalence of around 50% [3]. A significant proportion demonstrates reduced ionized calcium concentration [7]. Increased urea and creatinine due to concomitant renal disease is common in older cats.

Urinalysis - No classic changes but can rule out concomitant urinary tract infection and diabetes mellitus and enables the monitoring of urine protein.

Faecal analysis - Stools can be more voluminous, sometimes fatty due to increased transit speed or excessive fat intake due to polyphagia. Sometimes diarrhoea can be present.

Extended database

Diagnosis is straightforward with the demonstration of serum T4 concentrations > 50 nmol/l in most cases. Some cases have concentrations as high as 200 – 300 nmol/l. If the results are border line, the simplest approach is to wait 2 weeks and retest the T4 concentrations again. Some chronic and advanced cases or cats with concomitant disease may have T4 concentration depressed into the upper normal range by the principal of the sick euthyroid syndrome. These cases will usually still have an elevated free T4 (provided it is performed by the equilibrium dialysis method) and together with other classic clinical findings, should provide enough evidence to confirm the diagnosis. T3 suppression tests and TRH stimulation tests can be employed, but are laborious and usually superfluous. Scintigraphic evaluation (using pertechnetate) of the extent and location of thyroid tissue can be helpful in surgical planning and in confirming the diagnosis in cases with border line T4 and fT4 concentrations. Cervical ultrasonography has recently been used as an adjunctive tool in diagnosing thyroid masses and also to direct novel percutaneous injection therapy.

Treatment

The ultimate goal of therapy is the establishment of euthyroidism. This could be permanently achieved by either radioactive iodine injection or thyroidectomy. Cats can also be kept in a euthyroid state with oral medication. An antithyroid drug therapeutic trial should be instituted to monitor the effect of thyroid hormone reduction on kidney function, before using any of the above mentioned definitive treatments.

Oral medication with Felimazole® (Methimazole) or Neomercazole® (Carbimazole) at 2.5 - 5mg, respectively, two times daily, is usually instituted for the first 2 weeks. Thereafter the dose can be increased to 2.5 mg tid for felimazole and 5 mg tid for carbimazole for a further 2 weeks. Monitor serum creatinine concentrations before, at two weeks and after this therapeutic trial. If serum concentrations increase, the cat is
not a candidate for “permanent cure” with either radio-active iodine or thyroidectomy, because these may precipitate renal failure. Warn the owners regarding the precipitation of renal failure after treatment for hyperthyroidism. In short, the relative hypertensive state in hyperthyroidism increases GFR and therefore expedites the excretion of waste products and is somewhat renal-protective. If the GFR drops suddenly upon rectification of the problem, serum urea and creatinine concentrations may increase [8].

The decision to continue with drug therapy at 5mg once or twice daily for the rest of the cat’s life, is taken with due cognisance of this balancing act between amelioration of hyperthyroidism and maintenance of renal function. Some cats might need up to 15 – 20 mg/cat/day. Monitor serum T4 concentrations every 3-6 months if on drug therapy. Methimazole is also available in a topical formulation that can be used in cats that are hard to “pill”.

**Radioactive iodine** injection is a permanent cure, but its employment is contingent upon the availability of such specialist facilities and the willingness of an owner to part with his cat for a variable period of time whilst the cat is radio-active post treatment – up to 4 weeks in some countries. For similar reasons, it is near impossible to consider this form of therapy in a cat with serious concomitant disorders that will require daily medication and handling.

**Surgical thyroidectomy** is a relatively straightforward procedure in the hands of a competent and experienced surgeon. The parathyroid glands should be preserved if at all possible. Stabilise the animal first on carbimazole or methimazole for a 3 – 6 week period. Warn the owners regarding recurrence of the disease if all thyroid tissue could not be excised. If at all possible, attempt to remove both thyroid lobes. This however increases the risk of post-operative hypocalcaemia, which could be fatal if left untreated.

Percutaneous ethanol injection as well as percutaneous radiofrequency heat ablation are relatively promising new additions to the veterinarian’s treatment armoury [9,10].

**Possible complications of the most common therapies**

**Surgical thyroidectomy**

- Post-operative bleeding; Post-operative hypocalcaemia from day 3 onwards if the parathyroid glands were damaged; Hypothyroidism which is fortunately rare; Laryngeal paralysis due to damage to the recurrent laryngeal nerve

**Neomercazole**

- Bone marrow suppression; Facial pruritus; Vomiting; Anorexia; Hepatopathy

**Prognosis**

Prognosis is good after surgery, provided none of the complications have occurred. Normal lifespan could be expected. Hypertrophic cardiomyopathy, if solely due to hyperthyroidism, is often reversible. With drug therapy, the short-term prognosis is better, but in the long term it is difficult to achieve control and drug doses have to be increased. Patient and subsequent owner compliance declines as time wears on. Patients get increasingly reluctant to be pilled three times a day – some don’t tolerate it from the start.
References
4. Court MH, Greenblatt DJ. 2000. Molecular genetic basis for acetaminophen glucuronidation by cats: UGT1A6 is a pseudogene, and evidence for reduced diversity of expressed hepatic AGT1A isoforms. Pharmacogenetics 10, 355