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Feline Hyperadrenocorticism

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Feline adrenal diseases are uncommon compared to the dog. Despite a scarcity of reports, it is important to know these diseases are often fatal if not treated appropriately. Proper recognition and adequate testing are therefore crucial. Diseases with increased adrenal function are hypercortisolism, hyperprogesteronism and hyperaldosteronism. Only the first will be discussed, as the second two are even more rare (hyperprogesteronism reported in two cats, hyperaldosteronism reported in < 10 cats).

HYPERCORTISOLISM

So far less than 100 confirmed cases of naturally occurring, spontaneous, confirmed cases of hypercortisolism (Cushing’s disease) have been reported. More that 80% are due to a pituitary adenoma (very rarely adenocarcinoma) (PDH) while the remaining are commonly due to an adrenocortical tumor (equally divided between benign and malignant forms) (AT). There is no breed or sex predilection and most animals are older (mean 10 year, range 4.5-15).

Clinical appearance:

The most common historical and clinical signs associated with feline hypercortisolism are polyuria/polydipsia (PU/PD), polyphagia, weight loss and lethargy. PU/PD is mostly due to concurrent diabetes mellitus but can also occur in cats not being diabetic. The typical Cushing’s syndrome related pot-bellied appearance with hepatomegaly, weight gain and generalised muscle wasting is common in cats, as it is in dogs. Dermatological abnormalities frequently recognised in cats include an unkempt hair coat with patchy alopecia. In addition, extreme fragility of the skin is relatively common in cats; the thin skin may tear with routine handling or during playing with other cats, leaving large denuded areas. Infections and abscesses are seen in about 40% of cases and can be found in the urinary system, skin, respiratory tract or oral cavity.

Diagnosis:

A stress leukogram (lymphopenia, eosinopenia and mature leucocytosis) occurs inconsistently. Despite clinical PU/PD, cats usually maintain urine specific gravities of greater than 1.020; they only occasionally exhibit the dilute urine and decreased blood urea nitrogen concentrations commonly seen in dogs with hyperadrenocorticism. Hyperglycaemia (about 80%) and hypercholesterolaemia (about 50%) are the most common laboratory abnormalities found on serum biochemistries. In contrast to dogs, high serum alkaline phosphatase activity is uncommon, developing in only 32% of cats.

Diagnostic imaging shows hepatomegaly (about 80%) on plain radiographs and – if the case of adrenal tumour – sometimes a mass cranial to the kidney. However, calcification of normal adrenals can occur in up to 30% of normal old cats. Abdominal ultrasound is useful to detect bilaterally enlarged adrenals (in PDH) or a unilateral mass with contra-lateral atrophied adrenal. MRI might help to find a pituitary mass.

Endocrinological evaluation of cats suspected of hyperadrenocorticism involves screening tests to confirm the diagnosis, and differentiating tests to distinguish PDH from AT. For test protocol and normal values see Appendix. The ACTH stimulation has a sensitivity of about 80%; however, it can also give a positive result in ill cats with non-adrenal disease. However, values > 500 nmol/l are not commonly seen in these and point towards hypercortisolaemia.
Use of the urine cortisol-to-creatinine ratio (UCCR) appears have been commonly positive in cats with hypercortisolaemia; but false-positive test results may be seen in cats with moderate to severe non-adrenal illness. Urine should always be collected at home (not in hospital environment) as all stressful situations will elevate the UCCR. Sensitivity seems to be high, indicating that a normal value rules-out hypercortisolaemia.

The low-dose (0.01 mg/kg) dexamethasone suppression test provides diagnostic results that confirm the diagnosis (i.e. inadequate cortisol suppression) in almost all cats with hypercortisolaemia, but false-positive test results again will be seen in many cats with moderate to severe non-adrenal illness. Additional dexamethasone suppression testing using a higher dexamethasone dosage (0.1 mg/kg) has been advocated as a screening test; resulting in a sensitivity of 78%. Serum cortisol values in all normal cats and all cats with non-adrenal illness are suppressed with this dose.

A higher-dose (1.0 mg/kg) dexamethasone suppression test or basal endogenous ACTH concentration has been used to differentiate cats with PDH those with AT. Normal to high plasma ACTH levels support a diagnosis of PDH, whereas low concentrations are consistent with AT.

**Treatment:**

Potential options for treatment of cats with hypercortisolaemia include the use of the adrenocorticolytic agent mitotane (o,p’-DDD), drugs that block cortisol synthesis (ketoconazole, metyrapone or trilostane), unilateral adrenalectomy for AT, bilateral adrenalectomy or hypophysectomy for PDH, or radiation therapy for pituitary adenoma.

*Mitotane* is much less effective in cats than dogs and of 5 cats treated, only one responded. Higher doses might be necessary, but drug toxicity is not uncommon. 4 cats were treated with *ketoconazole* (5 mg/kg q12h for 7 days, then 10mg/kg q12h): 1 did not respond, one developed severe thrombocytopenia and 2 responded. *Metyrapone* has been used in 4 cats (65 mg q 8-12h): 1 did not respond, 2 had mild improvement and 1 was used to stabilise the cat before adrenalectomy. *Trilostane* has been used in 6 cats, all responded somewhat and showed improved endocrine test results. The dose of trilostane was similar to dogs (30 mg q24h as starting dose) and initial improvement occurred soon after starting. However, dermatological changes were always present to some degree and all diabetic cats, which initially required insulin, continued to do so.

In general, adrenalectomy appears to be the most successful mode of treatment for most cats, Unilateral adrenalectomy should be performed in cats with functional unilateral adrenocortical tumours, whereas bilateral adrenalectomy must be performed in cats with bilateral adrenocortical hyperplasia resulting from PDH. Cats undergoing unilateral adrenalectomy generally require glucocorticoid supplementation for approximately 2 months postoperatively, until the glucocorticoid secretory function of the atrophied contralateral gland recovers. By contrast, cats undergoing bilateral adrenalectomy require consistent, lifelong replacement of both mineralocorticoid and glucocorticoid hormones. Intraoperative and postoperative management of these cases is quite difficult and about 30% do not survive the first months after surgery (embolism, hypoglycaemic crisis, sepsis, etc.). Survival of cats with PDH after bilateral adrenalectomy is about 50% for the first six months. If cats survive that long and owner compliance (avoiding Addisonian crisis) is good, cats have a good prognosis. About 50% will no longer need insulin if they were initially diabetic. Hypophysectomy seems to be the best surgical treatment option (5 of 7 cats survived long term, insulin requirement dropped drastically or stopped altogether), however, this surgery is only available so far at few specialist centres (e.g. Utrecht University).

**Appendix** (reference values from Cambridge Specialist Laboratories, UK):

**ACTH stimulation test:**

Collect pre-ACTH serum sample for cortisol determination, then inject 0.125 mg/cat (i.e. half a vial) of synthetic ACTH (Synacthen) IV. Collect another serum sample after 60 minutes (some advocate also a third sample after 90 minutes).

Reference values:
- Baseline cortisol: 20-270 nmol/l
- Post ACTH cortisol: < 400 nmol/l
Dexamethasone screening test:

Collect baseline serum sample for cortisol determination, then inject 0.1 mg/kg dexamethasone (may need dilution) intravenously. Collect 2 post samples at 4 and 8 hours post injection.

Reference values:
- Baseline cortisol: 20-270 nmol/l
- 4-hour cortisol: <40 nmol/l
- 8-hour cortisol: <40 nmol/l

Urine cortisol-creatinine ratio:

Have owners collect urine at home from cat (non-absorbable litter) and have them bring to surgery. Centrifuge to clarify, draw off supernatant and ship in plastic tube to laboratory.

Reference values: < 10 x10^{-6}

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