Case report: feline acromegaly

Roisin O'Mahony MVB MRCVS Cert AVP (SAM) GPCERT SAM ESVPS, Animal Care Hospital, Douglas, reports on the possibility of acromegaly as a cause of diabetes mellitus in cats

INTRODUCTION

Acromegaly involves the excessive secretion of growth hormone (hypersomatotrophism). It is mainly caused by functional pituitary adenomas in the cat, though, occasionally hyperplasia of the pituitary can also occur (Berg, 2007). High levels of growth hormone decrease the available insulin receptors available and antagonise the peripheral effects of insulin on the body. This eventually leads to diabetes mellitus, which is commonly insulin-resistant. This report describes a case of acromegaly in a cat, which exhibited signs of insulin-resistant diabetes as well as changes to its facial structure. Growth hormone exerts anabolic effects on the body. Growth of the jaw, extremities of the body, and skull are frequent sequelae of acromegaly. Feline acromegaly is an emerging disease with prevalence among diabetic cats – one in three in North America and one in four in the UK (Berg, 2007; Niessen, 2007). This report highlights the importance of a thorough investigation of insulin-resistant diabetes and the possibility of acromegaly as a cause of diabetes mellitus in cats.

HISTORY AND PRESENTATION

A six-year-old, 8.2kg, male, neutered, domestic, shorthaired cat presented with polyurea and polydipsia. The owner also reported excessive snoring. There was normal appetite and energy levels. There was no history of trauma, access to toxins or foreign travel. Annual vaccines, worming and flea treatment were up to date. Clinical examination revealed obesity with a body condition score of 8/10. Mentation was normal. Heart rate was 152bpm, respiration rate was 30. Oral examination was normal. Upper respiratory tract examination was unremarkable with no abnormal respiratory noises. Mucous membrane colour was pale pink with a capillary refill time of <2 seconds. Superficial lymph nodes were normal. Abdominal palpation revealed no abnormalities. Body temperature was 38.1C. Ophthalmological examination and neurological examination were normal. Hydration was normal.

DIFFERENTIAL DIAGNOSES

Primary polydipsia:	**Psychogenic** **Hepatic insufficiency or porto-systemic shunt**
Primary polyurea	**Diabetes mellitus** **Hepatic insufficiency** **Renal disease – chronic renal failure, pyelonephritis** **Hyperthyroidism** **Hypercalcaemia** **Hypokalaemia** **Post obstruction diuresis** **Central or nephrogenic diabetes insipidus** **Drug induced** **Acromegaly**

Figure 1.

Polyurea and polydipsia are assumed to be linked. Possible causes in this case are outlined in Figure 1.
There was no history of drug consumption or of dysurea. Obesity assumed to be lifestyle related. Obesity increases the risk of diabetes mellitus and hepatic lipidosis in cats. Respiratory stertor was thought due to fat deposits around upper respiratory tract. Blood and urine sampling was required.

DIAGNOSTIC INVESTIGATION

A jugular blood sample was collected for haematology and biochemistry including electrolytes and thyroid hormone levels. Haematology was unremarkable. Biochemistry revealed marked hyperglycaemia with a blood glucose of 23.96mmol/l (4.1-8.8). Electrolytes and thyroid hormone levels were normal. Full urinalysis was carried out. Results showed marked glycosurea and low urine specific gravity (1.012).

Possible causes of hyperglycaemia include diabetes mellitus, stress hyperglycaemia, hyperadrenocorticism, and acromegaly. Diabetes mellitus was diagnosed given the marked hyperglycaemia and glycosuria, with low urine specific gravity due to renal medullary washout

INITIAL DIAGNOSIS

DIABETES MELLITUS

TREATMENT

Insulin treatment was commenced using protamine zinc insulin (Prozinc 40iu/ml, Boehringer) with 0.45 units/kg injected subcutaneously twice daily at the time of feeding. Client was counseled on insulin storage and administration and was observed to have good injection technique. A high-protein, low-calorie diet was commenced (Hills M/D).
Serial blood pressure measurements taken twice at four-week intervals revealed hypertension with an average blood pressure reading of 168/121. Treatment was commenced with amlodipine (Amodip, Interchem) at 0.17mg/kg sid orally. Blood pressure measurements two weeks post commencement of treatment were normotensive.
The cat was re-examined at two to three-week intervals over the following 12 weeks. Each time the owners described ongoing polyphagia. Body weight remained the same. Serial blood glucose curves and fructosamine measurements carried out each time showed inadequate response to insulin treatment with nadir blood glucose consistently >20mmol/l. Insulin storage and injection technique was discussed with the owner, there was no shortcomings found in the management at home. Insulin dosage was increased by 25% after each examination with an insulin dosage of 1.2iu/kg bid three months after commencement of treatment.
Three weeks later, serial glucose measurements showed a sub optimal response to insulin with nadir blood glucose of

22.7mmol/l (Figure 2). The patient was considered insulin resistant at this stage, given the consistent hyperglycaemia despite an insulin dose of >1iu/kg.

Causes of insulin resistance	
Problems with owner compliance	Check injection technique. Discuss diet.
Problems with insulin	Check in date, stored correctly, not shaken, correct syringes used.
Concurrent disease	Rule out obesity, pancreatitis, urinary tract infection, renal insufficiency, hyperthyroidism, oral infections, acromegaly, hyperadrenocorticism, pyoderma.
Insulin antibodies	Rare with use of protamine-zinc insulin.
Insulin over dosing and glucose counter regulation	Not evident from serial glucose curves.

Figure 2.

Clinical examination revealed prognathia inferior – protruding mandible and increased distance between the upper and lower canines and a broad face (Figures 3 and 4). Repeat haematology and biochemistry including thyroxine level were normal save for the persistent hyperglycaemia. Abdominal ultrasound carried out by a diagnostic imaging specialist was unremarkable. Urinalysis demonstrated glycosuria and negative bacterial culture.

A blood sample was collected for insulin like growth factor 1(IGF-1). IGF-1 value was significantly increased at >1,000mcg/ml (with values considered indicative of acromegaly at >598mcg/ml). A diagnosis of acromegaly was made due to the presence of physical changes consistent with acromegaly along with insulin resistant diabetes and increased IGF-1d.

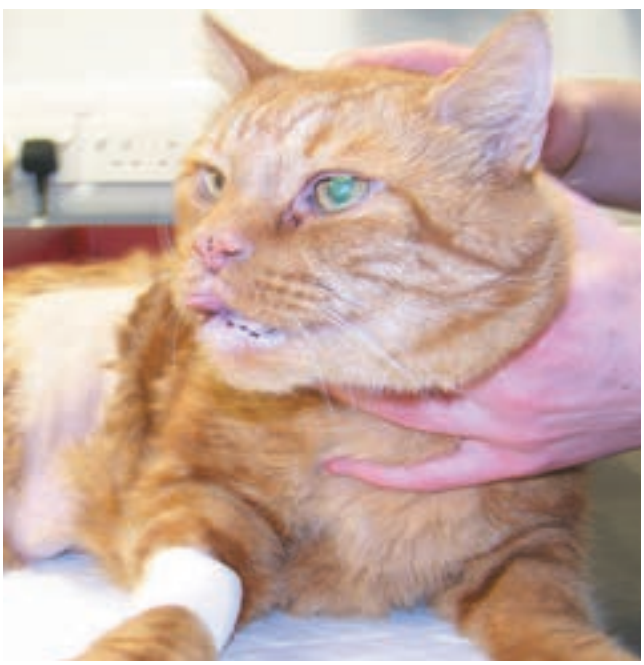

Figure 3: Example of prognathia inferior. Photo: RVC Diabetic Remission Clinic.

Figure 4: Example of prognathia inferior and broadening of face in feline acromegaly. Photo: Michael Herrtage BVSc DVSc MA DVR DVD DSAM DipECVIM DipECVDI MRCVS.

FINAL DIAGNOSIS

ACROMEGALY

OUTCOME

Treatment options were discussed including referral to the Royal Veterinary College for transphysysoidal hypophysectomy, radiotherapy or use of somatostatin analogues such as pasireotide (Signifor, Novartis).

The owners elected for symptomatic control, given financial constraints. An insulin therapy regime using a mixture of high doses of short-acting and long-acting insulin was initiated. Carbergoline (Galastop, CEVA) treatment was also started at 5mcg once daily to attempt to reduce IGF-1 levels. Two weeks later, the cat developed dyspneoa, suspected to be secondary to congestive heart failure. The owner elected for euthanasia.

CASE DISCUSSION

Acromegaly causes diabetes which is insulin resistant in 80% of cases (Nelson, 2009). A study documenting treatment of a group of acromegalic cats showed some cats receiving as much as 35iu insulin twice daily (Niessen, 2007). Respiratory stertor occurs in over half of acromegalic cats secondary to enlargement of the tongue and oro-pharangeal tissues (Niessen, 2007).

Protamine zinc insulin was chosen as part of the initial treatment regime due to its longer duration of action and lower mean blood glucose concentration in diabetic cats (Rucinsky, 2010; Sparkes, 2015). Hypertension is a relatively common consequence of acromegaly, both in human and in feline patients, with one study showing 20% of acromegalic cats experiencing hypertension (Myers, 2014).

This cat developed dyspnoea thought to be secondary to cardiac complications. There is a high incidence of cardiac dysfunction amoung acromegalic cats (Myers, 2014). The anabolic effects of IGF-1 cause enlargement of the heart as well as detrimental effects on the myocardium (Greco, 2012). Hypertension contributes to left ventricular hypertrophy and cardiac dysfunction.

There is no definitive test for the diagnosis of acromegaly. Diagnostic approach here included ruling out other causes of insulin resistance. Hyperadrenocorticism was thought unlikely due to lack of other characteristic dermatological signs or enlargement of the adrenal glands on ultrasound examination. However, the low dose dexamethasone suppression test could have served as a definitive rule out for this condition. Measurement of IGF-1 is an excellent

screening test for acromegaly in cats undergoing insulin therapy. Berg (2007) reports 84% sensitivity and 91% specificity for serum IGF-1 concentration as a diagnostic test for acromegaly in cats. Unfortunately, it is not useful for initial screening of untreated diabetic cats as many of them will have suppressed levels of IGF-1 (Ciftci, 2011). There is no commercially available feline growth hormone assay available currently.

Pituitary imaging will show evidence of pituitary tumours in the majority of cats with acromegaly. CT scanning was declined by the owners. Hypophysectomy is a curative treatment for acromegaly and the treatment of choice in human acromegaly. Many of the cats who undergo hypophysectomy also enter diabetic remission (Meij, 2010). However, the owners declined this on the basis of cost and travel difficulties.

Radiation therapy can achieve remission in the majority of cats with acromegaly. Studies have shown an improvement of neurologic signs and decreased insulin requirements or diabetic remission in treated cases (Kaser-Hotz, 2002; Mayer, 2006). Median survival of treated cats was 28 months (Dunning, 2009). Radiotherapy is less successful in reducing the growth of the tumour (Brearly, 2006).

Medical options for treatment include the use of a somatostatin analogue pasireotide (Signifor). Treated cats show a good improvement in diabetic signs and can enter remission (Gostelow, 2017; Scudder, 2015). However, this treatment is expensive and not without side effects. The use of carbergoline for feline acromegaly is safe and well tolerated but has not shown high efficacy in ongoing clinical trials (Scudder, 2018).

Long-term survival in acromegalic cats can also be achieved through symptomatic treatment. This involves the use of high doses of a mixture of long and short acting insulin along with strict feeding regimes and treatment of other clinical signs such as cardiac issues and joint problems (Peterson, 1990). However, there is a risk of hypoglycaemia with this approach. Also, in the absence of curative treatment most cats succumb to compilations of uncontrolled diabetes, congestive heart failure and joint issues over time.

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