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VDIC Case # 037-2014 Jan 5th, 2014 VDIC Consultant: David Bruyette, DVM, DACVIM



Referral Information:

A 16 year old FS domestic short hair cat was referred for insulin resistance diabetes. The current weight was 6.5 kgs. The patient was diagnosed with diabetes mellitus 3 months ago and insulin and a dietary change had been instituted. The cat was currently receiving 10 units of glargine (Lantus) insulin twice daily and there had been no improvement in clinical signs and on the most recent blood glucose curve the glucose values were never lower than 400 mg/dl. The patient was receiving no additional medications and had an unremarkable past medical history.

Physical Examination:

On physical examination no significant abnormalities were detected with the exception of mild hepatomegaly. The skin and hair coat appeared to be normal. A thyroid nodule was not palpated.

Initial Diagnostic Tests:

A recent CBC and chemistry panel had been unremarkable with the exception of a blood glucose of 410 mg/dl. (Data on file at VDIC; Case # 037-2014).

VDIC Initial Assessment:

By definition the patient is insulin resistant. Criteria for diagnosing insulin resistance include insulin doses > 1.5 units/kg per dose, fluctuating insulin requirements, persistent hyperglycemia (> 300 mg/dl during a blood glucose curve) and inconsistent control of clinical signs. Common causes of insulin resistance in the cat include hyperthyroidism, hyperadrenocorticism, acromegaly, and infectious disease. The most common cause of insulin resistance is felt to be acromegaly.

Suggested Plan:

Diagnostic: We would suggest the following diagnostic tests: A urine culture, a TT4 concentration, and a serum IGF-I concentration.

Therapeutic: Pending these test results I would continue the current dose of glargine insulin.



February 12th, 2014:

Results of the TT4 concentration were normal at 1.5 ug/dL. The urine culture was negative. The serum IGF-I concentration performed at Michigan State University was elevated at 325 ng/ml with normal values up to 90 ng/ml.

Final Assessment:

Insulin resistant diabetes secondary to acromegaly.

Treatment Plan:

Currently, treatment options for feline acromegaly include transsphenoidal hypophysectomy, radiation therapy (traditional or stereotactic), or continued use of high doses of insulin to correct the hyperglycemia. Of these options only surgery has been shown to normalize IGF-I concentrations. Radiation therapy has been shown to improve clinical signs of diabetes and reduce the size of the pituitary tumor. However cats in which IGF-I concentrations fail to normalize often die as a result of hypertrophic cardiomyopathy.

Case Follow-Up:

March 4th, 2014:

An MRI was performed which revealed a pituitary macroadenoma. The mass measures one by $1.2 \times 1.1 \times 1.4$ cm. The mass extends above the dorsum sellae. There does not appear to be any involvement of the carotid arteries or cavernous sinus. Based on the MRI scan both surgery and radiation therapy with seem to be appropriate.

March 6th, 2014:

The owner elected to proceed with definitive hyper fractionated radiation. The treatment will involve 16 fractions at 2.7 Gray per fraction. I would recheck the serum IGF-1 concentrations at 1 and 3 months and recheck the MRI in 6 months. In addition home monitoring of the blood glucose concentrations (preferably with the Alpha-Trak meter) is recommended as insulin requirements may change rapidly as IGF-1 concentrations decrease. Since the patient is receiving a basal insulin we do not need to perform a full glucose curve. We only need to obtain a pre meal/pre insulin blood glucose and a second sample 4 hours later.

April 10th, 2014:

The serum IGF-1 concentration was 184 ng/ml. The fasting blood sugar (obtained at home) was 214 mg/dl and the 4 hour post prandial was 234 mg/dl. I would reduce the glargine dose to 8 units BID and recheck the glucoses in 2-3 weeks. I would recheck the IGF-1 concentration in 2 months.

June 14th, 2014:

The serum IGF-1 concentration was 154 ng/ml. The fasting blood sugar (obtained at home) was 176 mg/dl and the 4 hour post prandial was 230 mg/dl. I would reduce the glargine dose to 6 units BID and recheck the glucoses in 2-3 weeks. I would recheck the IGF-1 concentration in 3 months as well consider a repeat MRI to assess tumor size.

July 1st 2014:

The fasting blood sugar (obtained at home) was 184 mg/dl and the 4 hour post prandial was 217 mg/dl. I would continue the current glargine dose of 6 units BID and recheck the glucoses in 1 month.

September 10th, 2014:

The patient is doing very well clinically and has no symptoms of diabetes mellitus.

An MRI was performed which revealed a pituitary macroadenoma. The mass measures 0.8 \times 0.9 \times 1.0 cm. The mass extends just above the dorsum sellae. There is evidence of hemorrhage within the mass and no edema is noted. I would recheck the MRI in 6 months (unless clinical signs or a rising IGF-1 concentration are noted).

The fasting blood sugar (obtained at home) was 146 mg/dl and the 4 hour post prandial was 211 mg/dl. I would continue the current glargine dose of 6 units BID and recheck the glucoses in 1 month.

Prognosis:

The majority of studies that have been performed in veterinary medicine focus on radiation treatment of pituitary masses regardless of functional status. There is no standard treatment protocol for pituitary masses in veterinary medicine and varying methods have been used including both single and multiple dose fractions administering total dosages ranging from 1,500 – 4,500 cGY. The majority of the cats included in these studies had insulin resistant diabetes (suspected acromegaly or Cushing's disease) and/or neurologic signs. Radiation therapy was shown to be successful in improving insulin resistance and neurologic signs. Neurologic improvement was generally seen within weeks to months and an improved insulin response was seen within the first month, however, most patients still required insulin therapy. In cases where repeat imaging was available a decrease in tumor size was also noted. Disadvantages of radiation therapy are the early and delayed effects of radiation, repeated anesthesia, and expense. Early effects from radiation therapy include hair loss, skin pigmentation and otitis externa. Reported late term side effects include brain necrosis, tumor regrowth, and visual and hearing impairment. In one study, 12 cats with pituitary tumors were treated with a coarse fractionated radiation protocol delivering a total dose of 37 Gy in 5 once weekly doses. Eight of these cats had insulin resistant diabetes mellitus secondary to acromegaly. Of these 8 cats, 5 no longer required insulin therapy,

2 became stable diabetics, and 1 required less insulin. In addition, 3 of 4 cats had improved neurologic signs. The mean survival time of cats in this study was approximately 18 months. In another study, 11 cats with pituitary tumors were treated with modified radiosurgery by delivering a single large dose (between 5-20 Gy) of radiation. Nine of the 11 cats had poorly regulated diabetes mellitus (acromegaly or hyperadrenocorticism). After treatment 5 (55.5%) had improved insulin responses and 2 of 2 cats with neurologic signs had improved clinical signs. The median survival time of cats in this study was 25 months.