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Insulinoma in Ferrets

Insulinomas (pancreatic beta islet cell tumors) are the most frequently encountered neoplasia in ferrets.¹



Middle-aged to older ferrets are more commonly seen with this disease; however, ferrets as young as 2 years of age can be afflicted. Because of the risk for potentially life-threatening hypoglycemic states, ferrets should be evaluated and screened for this disease before clinical signs are evident.

Clinical Signs

A pancreatic beta islet cell tumor produces insulin indiscriminately and is refractory to the subsequent negative feedback created by hypoglycemic and hyperinsulinemic states.

- The most common clinical signs of insulinoma are lethargy and hindlimb weakness. Other signs include mental dullness, irri-

tability, star-gazing, ataxia, ptyalism, or pawing at the mouth.

- Affected ferrets typically have a history of progressive lethargy and ataxia in the hind end, and owners report that they sometimes are difficult to rouse from sleep, tire easily, or easily lose their footing on slippery surfaces.
- If diagnosis is delayed, hypoglycemic patients may present comatose, obtunded, hypothermic, or in seizure.

Diagnosis

Blood Glucose

Ferrets as young as 2 years should be screened by obtaining a blood glucose level by a serum chemistry panel or a reliable veterinary glucometer. Severe hypoglycemia (glucose level < 60 mg/dL) after a 4- to 6-hour fast indicates insulinoma.

Care must be taken not to overinterpret a low blood glucose finding. It is not uncommon for a sick ferret that has not been eating well or at all to be hypoglycemic at presentation to the veterinary clinic. A low blood glucose level after an 8- to 10-hour fast is also not diagnostic for an insulinoma. However, if the ferret has eaten within 4 hours before having blood drawn and

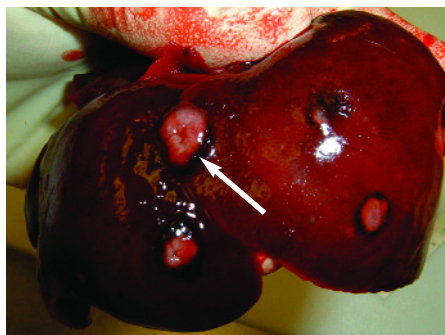
the blood glucose level is below the threshold (< 60 mg/dL), this can be considered a true indication of an insulinoma.²

Insulin

Plasma or serum insulin levels can also be investigated in ferrets suspected of having insulinoma. Elevated insulin levels (> 279 mU/mL) with concurrent hypoglycemia is consistent with hyperinsulinism and supports the diagnosis of insulinoma.³ However, a normal or low insulin level does not necessarily rule out an insulinoma if there is erratic production and secretion of insulin due to other underlying disease states.⁴ It is interesting to note that blood insulin levels are indicators for this disease in only about 80% of cases.⁵

Ultrasonography

Ultrasonography has been used to screen for pancreatic nodules, but it is not an ideal tool since many insulinomas do not produce nodules at all or produce nodules that cannot be recognized with ultrasound. In 1 study, only about 22% of confirmed cases had positive findings on ultrasonography.⁵



Insulinomas can metastasize and form functional islets (arrow) in other organs, such as the liver.

continues



Once an insulinoma has been diagnosed, frequent oral feedings (without carbohydrates) are important.

Surgery

Pancreatic islet cell tumors can occur as hyperplastic regions, carcinomas, or adenomas. Surgical exploration, including biopsy of abnormal pancreatic tissue, can be useful in diagnosis and characterization and such differentiation can guide further levels of care (eg, chemotherapy).

Levels of Care

Once insulinoma has been diagnosed, several treatment options are available. Currently there is a great deal of difference of opinion on opti-

mal therapy because no retrospective studies have compared therapeutic strategies and survival rates.

Nutrition

Diet modification is usually required to ensure successful treatment. The owner should be told to discontinue the use of sugary treats (eg, raisins, yogurt drops) and transition to a low-carbohydrate food (eg, Prescription Diet m/d Feline, www.hillspet.com; or EVO Ferret, www.naturapet.com). The ferret should always

have access to food; lack of food could result in a severe hypoglycemic state.

Medications

Prednisolone

The traditional option for medical treatment consists of daily doses of oral prednisolone to stimulate gluconeogenesis. A low dose of 0.2 mg/kg PO Q 12 H or 24 H can be used initially, but the dose must be tailored to both eliminate the clinical signs and achieve euglycemia.

Although prednisolone therapy will alleviate signs and restore a good quality of life, keep in mind that it will not reduce the growth of the primary tumor—the ferret will eventually become hypoglycemic again unless the glucocorticoid dose is readjusted. The prednisolone dose can be gradually increased as needed, but once it has reached approximately 2 mg/kg a second drug should be added to help control glucose levels.

Diazoxide

Diazoxide can be used either alone or in conjunction with prednisolone. This drug helps raise blood glucose levels by directly inhibiting pancreatic insulin secretion. It is available in a liquid form at a concentration of 50 mg/mL. The usual starting dose is approximately 10 mg/kg.⁶



Ultrasonography of the abdominal cavity can help visualize nodules in the pancreas but cannot be used to diagnose insulinoma.



Diazoxide can extend the efficacy of steroids for a reasonable length of time and, once it is started, the prednisolone dosage can usually be reduced. Remember that as with steroids, this drug will not interfere with the growth of the primary tumor; if “resistance” to the drug develops, hypoglycemia may recur.

Because of the multiple side effects associated with long-term use of steroids, it might be wise to offer the option of starting with diazoxide first instead of prednisolone. However, many owners shy away from using it as the first choice due to its high cost (about \$5–\$10 per mL).

Surgery

Surgical treatment is the other option. Excision of the nodules from the pancreas is straightforward, and a partial pancreatectomy is often performed at the same time. The latter combination therapy substantially prolongs the euglycemic state in the postsurgical period over nodule removal alone.⁷

Follow-Up

After the initial diagnosis of insulinoma, blood glucose levels should be rechecked every 7 days until a value greater than 80 mg/dL is achieved. A follow-up glucose assessment every 3 to 6 months is indicated to detect a hypoglycemic episode.

Client Education

It is imperative that owners be made aware of options before starting treatment protocols since medical therapy may result in drug resistance. It is important to help the owner understand that there is no cure for this disease and that it is ultimately progressive, necessitating changes in therapeutic strategies over time. However, many cases can be managed successfully for many months to years. It is also important to point out that other concurrent diseases (especially gastrointestinal disease) will often cause deregulation of a previously well-controlled insulinoma.

When to Consider Referring

Severe hypoglycemia in ferrets is a medical emergency, and these patients need 24-hour



With good ultrasonography equipment and skill, the pancreas can be visualized and examined for nodules.

care after being stabilized. Intravenous fluid therapy supplemented with dextrose 5%, along with periodic blood glucose monitoring, is important to prevent death. Patients with unmanaged insulinoma (or those receiving the maximum amount of prednisolone and diazoxide) are at risk for hypoglycemic episodes, and partial pancreatectomy may be the only treatment option once drug resistance develops. Ferrets with severe underlying disease should be referred for further testing because concurrent disease states (septicemia, starvation, liver disease) can also result in hypoglycemia and confound the diagnosis.

The Referral Process

Initial stabilization is required before the ferret can be transported to another facility. All relevant blood analysis and diagnostic images should be sent with the patient. Owners should be warned that treatment is life-long and that, if left untreated, insulinomas can result in death. The average monthly cost for prednisolone therapy alone is only about \$15. Increased costs are associated with initial or concurrent administration of diazoxide and periodic glucometer readings.

When Referral Is Not an Option

The primary goal for managing a ferret with insulinoma is correcting the hypoglycemic state. Hypoglycemic episodes usually resolve by correcting underlying fluid deficits, giving glucocorticoids to promote gluconeogenesis, and changing or providing an appetizing diet low in carbohydrates. The IV fluid of choice is lactated Ringers solution with 5% dextrose following intramuscular administration of dexamethasone. Once appetite is restored, administration of dextrose-supplemented fluids can be discontinued, and blood glucose levels should be rechecked approximately 4 hours later. If the ferret is not in hypoglycemic crisis, medical treatment can be started orally by the owner at home and the blood glucose levels checked in 1 week. The diazoxide and the prednisolone doses are adjusted according to the recurrence of the clinical signs. ■

See Aids & Resources, back page, for references, contacts, and appendices.

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