Hyperadrenocorticism in Ferrets

Basics

OVERVIEW
- Hyperadrenocorticism or ferret adrenal disease is a disorder caused by excessive production of sex steroids such as estrogens, androgens, and estrogen-related compounds by the affected adrenal gland or glands.
- Disease in the affected adrenal gland can be (1) hyperplasia, where it gradually enlarges and produces too much hormone but is benign; (2) adenoma, a benign, hormone-producing tumor; or (3) adenocarcinoma, a malignant, hormone-producing tumor.
- If benign, the tumor itself rarely causes problems, but the effects of the hormones it produces can be severe. They can cause prostate enlargement, hair loss or lack of hair regrowth, severe swelling of the vulva in females, cysts or abscesses of prostate tissue in both males and females, anemias, aggression, and/or muscle wasting.
- Malignant adrenal disease causes any or all of the symptoms described for benign disease. Additionally, the tumor itself can cause significant wasting and debilitation. It can invade into other organs into the abdomen and is eventually fatal.

SIGNALMENT
- Seen primarily in neutered animals—equal incidence in male and female animals. Females may be presented for evaluation more frequently than males because of the prominent appearance of vulvar swelling.
- Generally a disorder of middle-aged animals, 3–4 years old. The reported age range is 1–7 years.

SIGNS
- Severity varies greatly, depending on the duration and severity of sex steroid excess.
- Hair loss is the most common symptom. Hair loss may be sudden and progressive, or may begin in spring and regrow later in the year, followed by progressive hair loss the following spring. In most cases, hair loss is evenly distributed across the body, begins in the tail region, and progresses toward the front of the ferret. Other patterns, such as diffuse thinning of the hair coat over the shoulder region, can also be seen. In severe cases, the ferret will become completely bald. The skin usually has a normal appearance but can appear thickened.
- About 30% of affected ferrets are itchy; secondary bacterial skin infections are sometimes seen.
- Swollen vulva in spayed females is extremely common.
- Straining to urinate (due to prostate or “urogenital” cysts, abscesses, or enlarged prostate) can be seen in both
males and females. This can be a life-threatening consequence; large cysts can be visible as a focal swelling near the bladder.

- Sexual aggression or return of sexual behavior in neutered animals
- Thinning of the skin, muscle wasting, and pot-bellied appearance in long-term disease
- Occasionally, mammary gland (breast tissue) enlargement
- Rarely causes anemia, pale gums

**CAUSES**
Functional adrenal hyperplasia, adenoma, or adenocarcinomas

**RISK FACTORS**
Evidence suggests that adrenal disease may be related to neutering at an early age.

**TREATMENT**

**APPROPRIATE HEALTH CARE**
- Ferret adrenal disease may be treated with surgical removal of the gland, or managed medically. The decision as to which form of treatment is appropriate is multifactorial; which gland is affected (left vs. right), severity of clinical signs, age of the animal, other simultaneous diseases, and financial issues should be considered.
- Surgical removal of the affected adrenal gland(s) is often curative, although in rare cases, disease develops in the remaining gland.
- Medical treatment (see medications, below) may cause a reduction in or eliminate symptoms. Depending on the circumstances, medical treatment may be preferred. However, medical treatment is not curative, must be administered lifelong, and has no effect on adrenal tumor size or potential spread.
- If clinical signs are limited to cosmetic appearance (hair loss), some owners may elect not to treat at all. Be aware that metastasis (spread of cancer) does occur; the debilitating effects of the tumor itself may become significant.
- Hospitalization is usually required for ferrets with urinary tract obstruction due to prostate disease, severely ill ferrets, and during postsurgical recovery period for those undergoing surgery.

**ACTIVITY**
No alteration of activity necessary

**DIET**
Usually no need to alter diet

**SURGICAL CONSIDERATIONS**
- Surgical removal is the only way to completely get rid of this tumor. In most cases, the tumor is removed and does not return. This cures all of the effects of the tumor and the tumor itself. In some cases, especially if the right adrenal gland is diseased, the tumor has invaded into surrounding structures that cannot be removed. If this is the case, parts of the tumor that can be safely taken are removed. Symptoms go into remission but will eventually return.
- Occasionally, tumors develop in the opposite or remaining adrenal gland after surgery, and symptoms return.

**MEDICATIONS**
Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered all-inclusive.

**Lupron**
- Leuprolide acetate (Lupron) blocks the effects of excessive sex steroids on the skin, prostate, genitals, and other targets, thereby alleviating symptoms of adrenal disease. It is administered by injection every 4 weeks until signs resolve, then every 4–8 weeks as needed to alleviate symptoms, lifelong. This drug has no effect on adrenal tumor growth or spread. Most ferrets will regrow hair and stop itching, and other symptoms such as swollen vulva, weight loss, and aggression may improve. Not all ferrets improve with this medication, and eventually it may not help at all.
- Other similar medications such as deslorelin acetate (Suprelorin, goserelin (Zoladex) are available as low-release implants, and have been reported to be as effective as leuprolide acetate, with alleviation of symptoms lasting from 8 to 20 months.
Melatonin Implants

- Melatonin implants (Ferretonin, Melatek, LLC) can alleviate symptoms of adrenal disease such as alopecia, itching, aggressive behavior, vulvar swelling, and prostate enlargement. Implants are repeated every 4 months as needed, lifelong. Other than lethargy at high doses, very few side effects have been reported. As with Lupron and deslorelin, melatonin has no demonstrated effect on adrenal tumor growth or spread. Melatonin can be used simultaneously with Lupron in treatment of refractory cases. Oral administration of melatonin has also been used to temporarily control clinical signs, but it loses effectiveness after 12 months of continuous use.

Other Medications

- Other medications that block the effects of excessive hormones include flutamide, anastrozole, and bicalutamide. This are usually used in ferrets that no longer respond to Lupron or Ferretonin.

FOLLOW-UP

PATIENT MONITORING

- Response to therapy is evident by remission of symptoms, particularly hair regrowth, regression of vulvar swelling, and reduction in the size of prostatic tissue.
- If medical therapy alone is elected: Medical therapy has no effect on the growth of the tumor but simply masks symptoms of the disease. Recheck regularly with your veterinarian to monitor growth of the tumor (often evaluated with ultrasound examination).
- Recheck regularly with your veterinarian to monitor serum glucose (blood sugar) concentrations following surgery, since many ferrets have concurrent insulinomas (tumors of the pancreas that produce excess insulin) and develop postoperative hypoglycemia (low blood sugar).
- Following adrenal surgery, monitor for return of symptoms since tumor recurrence may occur. Clinical signs typically develop 1 year or more postoperatively.
- In ferrets in which both adrenal glands have been surgically removed, monitor for the development of Addison’s disease (lethargy, weakness, not eating, periodic blood work for electrolytes).

PREVENTION/AVOIDANCE

- There is some evidence suggesting that neutering after 6 months of age may decrease the incidence of disease.
- Yearly administration of Lupron or melatonin may prevent the onset of symptoms; tumors may continue to grow despite this treatment.

POSSIBLE COMPLICATIONS

- Recurrence of tumor or development of tumor in the remaining gland in patients that have had surgical removal of adrenal gland
- Metastasis (spread of cancer) in patients with carcinomas
- Weight loss and muscle wasting due to the energy draining effects of malignant cancers
- Development of postoperative low blood sugar in patients with undiagnosed insulinoma

EXPECTED COURSE AND PROGNOSIS

- Response to medical therapy may vary with tumor type. Some ferrets live normal healthy lives with medical treatment alone. Others respond minimally or stop responding after repeated treatments. Some ferrets require combinations of medical treatment to keep symptoms in check. None of the medical treatments will stop the growth of the tumor, if it is malignant. Rechecks with your veterinarian are important to monitor tumor growth.
- Ferrets with benign disease (adrenal hyperplasia or adenomas) will generally live 2 or more years, even with no treatment. Skin and genital symptoms will worsen without treatment.
- With malignant cancers, tumor growth can be rapid (weeks to months) and eventually result in serious and life-threatening disease. If metastasis occurs, the prognosis is poor.
KEY POINTS

- Ferret adrenal disease is one of the most common disorders diagnosed in pet ferrets, and is the leading cause of hair loss.
- The diseased adrenal may be benign or a malignant (cancerous) tumor. The only way to know if the adrenal gland is a malignant tumor is via a surgical biopsy. If surgery is not elected, ultrasound examination of the gland is often a good predictor of malignancy.
- The only permanent cure for adrenal disease is surgical removal. Even with surgery, some tumors return, or tumors develop in the opposite gland.
- Many ferrets with benign adrenal disease live normal, healthy lives with medical treatment alone. If using medical treatment, lifelong therapy is required.