Adrenal Gland Disease of Ferrets

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Introduction/Definition

Ferret adrenal gland disease or hyperadrenocorticism is one of the most common syndromes in middle-aged to older ferrets. The adrenal glands are a pair of organs that lie next to the kidneys and produce many important hormones, including sex steroid hormones. In ferrets, adrenal disease differs from the adrenal diseases affecting dogs and horses, known as Cushing's disease, hyperadrenocorticism, or pituitary pars intermedia dysfunction, in that it is associated with the overproduction of sex hormones (androgens) rather than natural steroids (glucocorticoids). Despite what the name implies, there is more than one type of ferret adrenal disease, and it can affect one or both adrenal glands. The adrenal gland may be affected by increased cell production (hyperplasia), benign cancerous growth (adenoma), or malignant cancerous growth (adenocarcinoma). The structural changes to the adrenal gland are associated with an increase in one or more sex hormones and the clinical signs or symptoms that we observe.

QUICK FACTS

- **Adrenal disease typically affects ferrets aged 3 years and older.**
- **Common signs include hair loss and itchiness.**
- **Medical therapy helps to manage clinical signs.**
- **Surgical therapy can reduce the clinical signs and potential mass effects.**
- **Prophylactic treatment of adrenal disease may be recommended by your veterinarian.**

Clinical Signs and Symptoms

Ferret adrenal disease is typically seen in individuals 3 years of age and older, but may be seen in ferrets as young as 2 years old. Clinical signs or symptoms are directly related to the overproduction of sex hormones. Some are specific to ferret adrenal disease, while others may be present with other diseases as well. Adrenal disease is most commonly characterized by symmetrical hair loss, which can start at the tail but worsen to affect the dorsum (back), itchiness, vulvar enlargement (females), straining to urinate (males), and increased sexual or aggressive behaviors (such as dragging cage mates).

Common Signs:

- Hair loss (alopecia)
- Itchiness (pruritus)
- Vulvar enlargement (females)
- Straining to urinate (males)
- Sexual and/or aggressive behaviors

Non-specific Signs:

- Weight loss
- Reduced activity (lethargy)
- Rear leg weakness

Alopecic ferret

Diagnostics

A diagnosis of ferret adrenal disease is based on the combined results of many different tests. No single test result is evaluated alone. The results of the tests listed below may be used together to evaluate what is best for your ferret. The history provided by you, the owner, along with certain physical examination findings, can be highly suggestive of adrenal disease. A ferret adrenal endocrine blood panel can indicate which hormones, if any, are elevated. An abdominal ultrasound can detect and measure enlarged adrenal glands and identify prostate changes in males. Finally, your veterinarian may recommend complete bloodwork and radiographs

(x-rays) to evaluate your ferret's overall health. It is not uncommon that the results of these diagnostics may be suggestive of other concurrent diseases, which may affect treatment recommendations.

Key diagnostics

- Physical examination
- Basic bloodwork
- Radiographs (x-rays)
- Ultrasound
- Endocrine panel

Treatment

Adrenal disease can be treated in two ways: surgical removal of the affected adrenal gland(s), or medical management. The best treatment for your ferret will depend on many factors, including age and other health problems.

Surgical removal of diseased adrenal tissue, or adrenalectomy, can be considered for ferrets that also possess another condition that would benefit from surgery, such as insulinoma, and are good candidates for anesthesia. Geriatric ferrets or ferrets with heart disease are not good candidates for surgical therapy. After surgery has been performed, the prostate gland will usually decrease in size in 2-3 days, while an enlarged vulva will decrease within days to 2 weeks. It will take longer (up to a few months) for signs of hair regrowth to be observed. The surgical complication rate is reported to be 5% within the first 24 hours, and the mean time to return of clinical signs is 13.6 months. A complication of complete adrenal gland removal is the development of other hormonal diseases (such as hypoadrenocorticism). Therefore, monitoring of your ferret post-surgery is needed. As most surgical removal of adrenal tissue is incomplete, medical hormonal suppression is warranted.

Medical therapy for ferret adrenal disease has fewer risks compared to surgery but does not cure the disease, reduce tumor growth, or reduce the risk of metastasis. Medical management does slow the disease and control most of the clinical signs. While medical management can control clinical signs in most patients, some may have treatment failures that require pursuing other treatment options.

Medical therapy commonly includes the use of gonadotropin (sex hormone) releasing blockers, such as deslorelin and/or leuprolide acetate. Deslorelin implants (Suprelorin-F, Virbac), suppress the stimulation of the portion of the adrenal glands that produce sex steroid hormones. After a deslorelin implant is placed, signs associated with adrenocortical disease may worsen during the first 2 weeks. Vulvar enlargement and itchiness usually decrease 10-14 days after treatment, and the vulva should return to a normal appearance by 6 weeks post-treatment. Hair regrowth typically occurs within 4-6 weeks post-implantation. Most ferrets have complete hair regrowth by 8 weeks post-treatment; however, regrowth can be incomplete in some individuals. Medical management with deslorelin therapy can last an average of 16.5 months before signs return.

Leuprolide acetate depot (Lupron) may also be used, but its effects depend on the formulation. Lupron 30-day depot is effective for

downregulating sex steroid production for about 30 days, and the Lupron 3-month depot formulation may last a median of 3.8 months with a range of 75-90 days in males and 60-75 days in females. Lupron is sometimes combined initially with a deslorelin implant, as it will act more quickly than the implant.

Your veterinarian may discuss other medications such as melatonin, anti-steroidogenics, and androgen inhibitors. Melatonin (Ferrotonin, Maletek LL) has been demonstrated to alleviate clinical signs but does not significantly reduce sex steroid production. Therefore, there is continued release and growth of the adrenal tumors with this treatment option. Trilostane is an anti-steroidogenic medication that prevents the production of corticosteroids. It is commonly used in the treatment of hyperadrenocorticism (Cushing's disease) in dogs. It was tried to treat adrenal disease, however it caused extreme suppression of other adrenal hormones, which was life-threatening. Therefore, treatment with trilostane is not recommended. Flutamide, another medical option, is an androgen inhibitor that may be used in initial treatment specifically to reduce prostate enlargement in affected male ferrets. Other medications for reducing prostate size in males include bicalutamide, finasteride, and anastrozole.

If left untreated, advanced adrenal disease can cause serious, potentially fatal problems, including urinary obstruction in males or, in rare cases, bone marrow suppression and anemia. If a malignant adrenal tumor (adenocarcinoma) is present, it can spread to nearby organs. The mass effect from enlarged glands can compromise other abdominal organs and cause pain. Regular examinations along with monitoring diagnostics (such as ultrasonography) are recommended to monitor ferrets with adrenal disease.

Risk to Others

Ferret adrenal disease is not infectious or transmissible to other organisms.

Risk Factors

The cause of adrenal gland disease in ferrets is unknown, though it is speculated that neutering or spaying at a young age may play a role in causing the adrenal glands to assume the role of producing sex hormones. This theory arose because most ferrets in the United States are neutered or spayed before the age of 6 weeks, and a high incidence of the disease is noted in these ferrets. However, the incidence of adrenal tumors in European countries where ferrets are neutered and spayed between 8-11 months is similar to rates in the United States. This suggests that there is an alteration in the feedback of hormones after neutering or spaying that causes persistent stimulation of the adrenal cortex, regardless of the age of the neuter. Other potential factors that have been proposed include diet, genetics, and photoperiod, or the light/dark cycle.

Prevention

While surgical neutering may have some role in the development of ferret adrenal disease, it is important for the prevention of life-threatening hyperestrogenism that intact non-breeding female ferrets develop. As an alternative to surgical neutering alone, chemical castration with deslorelin or placement of a deslorelin implant before the development of symptoms of adrenal disease has been proposed.

Chemical neutering involves the placement of a deslorelin implant instead of surgery and is effective for between 1 to 3 years for both males and females. The adverse effects of chemical neutering are minimal and typically involve temporary scabbing or itching of the implant site. Unpublished data suggests a significant difference in the adrenal volume and circulating sex hormones between surgical and chemically neutered ferrets, with surgically neutered ferrets having larger adrenal volumes and higher circulating sex hormones. Additionally, unpublished research suggests that surgically neutered ferrets have twice as many adrenal adenomas as chemically neutered ferrets.

Surgically (left) and chemically (right) castrated male ferrets

The prophylactic placement of deslorelin implants and its long-term effect on the development of ferret adrenal disease is currently under investigation. However, based on the differences in circulating sex hormones between surgical and chemically neutered ferrets, your veterinarian may still recommend placing a deslorelin implant yearly before the development of obvious symptoms.

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