Introduction

When it comes to diagnosis and treatment, ferrets are just as complicated as our other four legged companions. There is a subset of diseases that are quite common among them though. Having a logical thought process and an in depth knowledge of these diseases, makes ferret medicine challenging and enjoyable. Adrenal disease, insulinoma, and lymphoma are the focus of this discussion.

Adrenal Disease

Adrenal disease is usually seen in middle aged ferrets, but can be seen at almost any age. This is not related to Cushings Disease. A hyperplastic or neoplastic process occurs in the cortical cells of the adrenal gland. Then cortical cells secrete excess sexual hormones, most commonly androstenedione, estradiol, and 17alpha-hydroxyprogesterone. The clinical signs correlate to the excess hormone secreted. Incidence has been reported to be as high as 80%. Some theories as to why this occurs include early spay or neuter, varying photoperiods, and genetics. It's likely that many factors are involved, but ultimately we do not know the cause.

Presenting complaint
- alopecia particularly on the tail and dorsum
- swollen vulva
- pruritus
- aggression/mothering
- hematuria/stanguria
- weight loss
- lethargy

Physical examination
- alopecia is by far the most common physical finding
- females can have a swollen vulva
- scabs on skin
- a large bladder can be palpated in males with prostatic enlargement
- splenomegaly
Diagnosis

- clinical signs and examination get us the diagnosis, but looking at the whole clinical picture is important
- complete blood count and biochemical analysis helps look for concurrent disease or bone marrow suppression from high levels of estrogen from the adrenal tumor
- radiology can assist us if blood or examination reveals concurrent disease
- ultrasound can identify the affected adrenal gland in addition to other disease
- hormone assays measure androstenedione, estradiol, and 17alpha-hydroxyprogesterone
- exploratory and histopathology

Treatment

There are many therapies available to manage adrenal disease in the ferret. This disease should be viewed as a managed disease, because a long term, complete cure is not common.

Medical

1. Leuprolide (250mcg)

Leuprolide is a GnRH agonist and inhibits the formation and release of FSH and LH from the pituitary by interrupting the normal pulsatile flow of GnRH and overloading and desensitizing the receptors. This subsequently decreases estrogen and androgen levels. It will keep smaller masses in control for a period of time as it can decrease their size in some patients. It can last 1-4 months depending on type used. It can be a great adjunct to surgery, particularly in those patients with prostatic enlargement or bone marrow suppression.

2. Deslorelin Implant (4.7mg)

Deslorelin is another GnRH agonist, but gives an initial surge of LH secretion. The implant can last up to 1 year. With this prolonged exposure it stimulates GnRH receptors, which in turn down-regulates and reduces gonadotropin release and subsequent reduction in circulating sexual hormones. It is administered subcutaneously and between the shoulders like a microchip. The implant releases medication and dissolves over time.

3. Androgen receptor blocker/Aromatase inhibitors (flutamide/anastrozole)

These medications are usually used in conjunction with other medical therapies or surgery. They can be helpful alleviating signs while other modalities take effect. They do not decrease tumor size.
Surgical

The left adrenal gland is located cranial to the kidney, just off the midline near the caudal vena cava. The left adrenal has the adrenolumbar vein coursing over its ventral surface. The right adrenal gland is found after the hepatorenal ligament is incised and the caudate lobe of the liver is retracted. The right adrenal gland is intimately attached to the caudal vena cava. Both glands should be approximately 2-3mm wide and 6-8mm long.

Abnormal glands will be enlarged, discolored, cystic, and be surrounded by hemorrhagic fat, or encompass other structures. Always compare the adrenal glands to each other.

Removal of the left adrenal is straightforward. This is considered and extracapsular technique as we do not need to enter the adrenal capsule. Dissect the fat that surrounds the gland and place the hemoclips on major vessels. Other vessels may grow to supply larger adrenal masses.

Removal of the right adrenal can be rather complicated. There are two main techniques for removal of the gland, extracapsular and intracapsular.

Extracapsular Technique

1. To remove the right adrenal gland completely it involves ligation of the caudal vena cava. This is only done in extreme cases. Usually this is necessary when there is invasion of the vena caval lumen. This is a two surgery technique. The surgeries are separated by four to twelve weeks, with six weeks to be seemingly ideal. Time is usually case dependant. At the first surgery, an ameroid ring or other constricting device is placed around the vena cava caudal to the adrenal gland. Routine closure follows. During the six weeks between surgeries, the vena cava begins to decrease in diameter. Collateral circulation develops, so at the next surgery, the vena cava can be completely ligated cranial to the adrenal gland and caudal to the constricting device to remove the invading adrenal mass. The reason this works is that collateral vessels have formed. There may be some evidence of these vessels at the time of the first surgery as the mass may have already started the process. The post-op care can be intensive with this procedure. Intravenous fluids, force feedings, and general care for the debilitated animals may be needed for many days after a vena caval ligation.

2. Venectomy and/or resection and anastomosis of the caudal vena cava can also be performed. While some of these techniques had their place, the development of the technique described above has all but eliminated their need.

3. Laser/Cryosurgery can be used for adrenal gland surgery. These methods are operator dependant. Get comfortable with a technique and then use it.
Intracapsular Technique

Apply a hemoclip to the base of the adrenal gland where it meets the vena cava for hemostasis. Incise the adrenal capsule with the iris scissors. Remove the adrenal tissue with a cotton swab or ophthalmic hemostat. Cut away excess tissue included the adrenal capsule above the hemoclip. This technique minimizes the tissue left behind and damage to the vena cava.

Both glands could be completely removed, and there may still be some aberrant adrenal tissue located in the abdomen. This is thought to occur in roughly 25% of ferrets. Since we cannot see microscopically at the time of surgery, we can easily leave some adrenal tissue behind. That is not necessarily a bad outcome. Some adrenal tissue is needed for blood pressure and water regulation, and steroid production. I regard surgery as the primary mode of therapy, followed by medication to manage clinical signs if needed. This is not unlike managing a malignancy. Use surgery to debulk the tumor, and follow with chemotherapy. Chemotherapy, in this case would be the medications described earlier. Ultimately, the appropriate treatments depend upon the extent of the adrenal disease, concurrent disease, surgeon comfort level, and budget for the owner.

Insulinoma

Insulinoma is a benign neoplasm of the beta islet cells of the pancreas. As the name suggests, they secrete insulin. The average age of onset is four to five years old, but can occur at almost any age. The incidence of insulinoma in ferrets is very high.

Presenting complaint
- lethargy
- weight loss
- ataxia
- ptyalism
- staring
- seizures

Physical examination
- Can be normal unless other diseases present
- Thin

Diagnosis
- glucose below 70mg/dl is suspicious for disease
- many times a fasting glucose is needed and be performed on serum
- insulin/glucose ratio – in normal animals if there is a low glucose, insulin production should decrease dramatically. Insulinomas will demonstrate a low glucose with high insulin levels
- as a general rule, we check blood glucose regularly starting at four years of age
• be mindful that most glucometers read 10% lower than the actual glucose
• also, glucometers can give a lower result with hemoconcentrated samples (HCT>55%)
• radiographs and ultrasound will identify concurrent disease; ultrasound can identify insulinomas
• exploratory and histopathology

Treatment

A similar philosophy to adrenal disease should be taken with treatment of insulinoma. We will be able to debulk the tumor, but there will be other insulinomas that are microscopic. They will develop over time, particularly when the excess insulin from one insulinoma is removed. That excess insulin from one can suppress other insulinomas. If medical treatment alone is used, the average period of control is about a year. If surgery and medications are used, the average life span increases to almost two years. Then combinations of medical and surgical therapy can increase quality and quantity of life beyond the two year mark.

Medical

Prednisone (0.5-2.0 mg/kg BID) acts as a hyperglycemic through its action as a glucocorticoid. Initially, we usually see a very good response. At the higher doses of prednisone we may see immunosuppression with prolonged use. The most common complications of immunosuppression are urinary tract infections and prostatitis. The reason we see prostatitis so often is that many ferrets will also have concurrent adrenal disease.

Diazoxide (5-10 mg/kg BID initially but can increase to 30 mg/kg) is another useful medication. It raises the blood sugar in a different way from prednisone by inhibiting secretion of insulin from the pancreas. Diazoxide is quite potent at opening K+ channels. The flow of K+ out of the beta islet cells keeps insulin in those cells and prevents it from being secreted. This medication can help to reduce the amount of prednisone, which is helpful in cases of immunosuppression. It also can be added later in disease management if prednisone is no longer working well alone. Diazoxide does have to be compounded and can be expensive.

Surgical

As with any exploratory surgery, develop a systematic approach to examine all parts of the abdomen. As we have discussed, many ferrets will have adrenal disease or other pathology concurrently. When evaluating the pancreas, be sure to examine the dorsal and ventral aspects of both the right and left limbs. Handling or surgery of the pancreas rarely causes pancreatitis in ferrets. Insulinomas will generally look like white firm nodules around 0.5mm-2mm in diameter. There are two main ways to remove insulinomas. They
can be removed individually or with part of the pancreas. Samples are sent for biopsy to confirm the correct tissue was obtained and to ensure there is no concurrent disease. During surgery ferrets are kept on intravenous fluids containing 5% dextrose.

**Insulinomectomy**

If there is a single or a few individual masses, they can be dissected out of the pancreatic tissue. Iris scissors work well to dissect and remove insulinomas. The area can then be closed with a fine monofilament dissolvable suture, if needed. Typically these patients stay in the hospital on intravenous fluids for one day. Glucose is monitored a few times post surgery.

**Partial Pancreatectomy**

Occasionally there are so many insulinomas in one limb of the pancreas that a partial pancreatectomy is needed. When there are numerous insulinomas many times there are one or two larger ones with many smaller ones. Isolate the limb of the pancreas for removal. Bluntly dissect with iris scissors to the vessels. Ligate vessels with a fine monofilament dissolvable suture. Typically for partial pancreatectomies the ferrets stay in the hospital for a few days for monitoring. Fluid and nutritional support with antibiotics will be helpful during their stay.

**Lymphoma**

Lymphoma is the most common neoplasia after adrenal tumors and insulinomas. There are a few different forms that can affect ferrets of all ages. The most common is the lymphocytic form of adults. It usually affects the peripheral lymph nodes, but can be infiltrative to different organs. The lymphoblastic form generally occurs in juvenile ferrets. This is more of an infiltrative disease to various organs, commonly the liver, spleen, and thymus.

**Presenting complaint**
- signs can vary depending on organ affected
- lump(s)
- lethargy
- anorexia
- diarrhea

**Physical examination**
- weight loss if chronic
- lymph node enlargement
- organomegaly (spleen/liver)
- respiratory difficulty (thymus)
Diagnosis

- complete blood count may have a lymphocytic shift (40% or greater of WBC’s)
- serum biochemistries may show affected organ
- radiographs may show masses or organomegaly
- ultrasound can be suggestive
- cytology may show lymphocytic or lymphoblastic forms
- histopathology

Treatment

Prednisone (2.2 mg/kg SID) can be used to give an initial good response for those clients that do not elect chemotherapy. This may send ferret into a short lived remission, but likely it will make them feel better temporarily, if at all.

Chemotherapy protocols are the best chance to send lymphoma into remission. There are many protocols with varying degree of effect. Pick one you are comfortable using. Response is dependent upon the type of lymphoma and concurrent disease. Typically the response is poor, but survival times seem to be longer with chemotherapy. Medications used are dependent upon availability of the chemotherapeutic agent, ability of veterinary staff, and cost. The ability to place an indwelling intravenous catheter may limit agents used. Typically a 24-27 gauge catheter is used to deliver medications that require intravenous access.