

NEW FERRET TRICKS: EMERGING DISEASE PRESENTATIONS

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The domestic ferret, *Mustela (putorius) furo*, is a highly inbred animal that is extremely popular as a pet. In the past 10 years, there has been a large increase in the number of pet ferrets available in pet stores in the United States. Predominantly they are from one commercial breeder, but there are other commercial breeders and small, individual breeders as well. Most of the diseases discussed are being seen in ferrets from different sources, although in the pet trade different shipments may be mixed. There has also been a move by all suppliers to neuter/spay and descent the ferrets at 3 to 4 weeks of age. The implications of surgery at that age on the immune system and disease exposure has not been studied (or at least appeared in the published literature). The alterations to the growth and development of the ferret may also be affected (as is being studied with adrenal disease). Regardless, this practice will continue. Ferrets are shipped usually at 6 to 8 weeks of age, and usually they have received only one vaccination, canine distemper. They are due for the rest of the series, and most do not get it, as pet stores repeatedly (erroneously) tell people "they've had their shots." Completion of distemper vaccination and rabies is frequently done after the ferret is 6 months to a year old, or has developed other medical problems. Most pet ferrets during their lifespan will develop dental disease, neoplasia, cardiomyopathy, and some form of gastrointestinal disorder. The pet ferret has one of the highest tumor rates of any mammal. These serious illnesses are in addition to the usual ferret follies: ear mites and trauma of multiple types. We do advise ferret owners to establish a savings account for their ferret's medical needs.

Many of the disease problems we are currently seeing need to be characterized and studied. Practitioners with cases are encouraged to tabulate their data and coordinate this with the pathologists or clinicians trying to discern the etiology, treatment, and prevention. Networking through online veterinary exotics discussion groups is extremely helpful as it establishes a pattern from which we can look at epidemiology.

FERRET INFECTIOUS PERITONITIS (CORONAVIRUS-FIP)

Ferrets are susceptible to coronavirus infections: experimentally to SARS (severe acute respiratory syndrome) and FECV (ferret enteric coronavirus). FECV is the cause of epizootic catarrhal enteritis (ECE) in ferrets. Lesions are only in the gastrointestinal tract, with virus found in the saliva, feces, and enterocytes. Feline coronavirus (FCOV) is responsible for a feline enteric self-limiting disease and the mutated form is responsible

for feline infectious peritonitis (FIP). The agent responsible for the "FIP-like" disease in ferrets appears to be a variant of the FECV virus, and is being called ferret systemic coronavirus (FSCV). Gross, histologic, and immunohistochemical features of FSCV are identical to FIP.^{1,2}

Clinical signs include weight loss (in some severe), anorexia, palpable intra-abdominal mass or masses, lethargy, vomiting, splenomegaly, dehydration, bruxism, renomegaly, sneezing/nasal discharge, systolic heart murmur, urine discoloration, dyspnea, peripheral lymphadenomegaly, rectal mucosa erythema, rectal prolapse. Central nervous system signs are seen in some ferrets and include acute or progressive hind limb paresis or paraparesis, ataxia, seizures, abnormal posture, opistothonus, abnormal gait, and proprioceptive deficits. Some ferrets have fevers ranging from 103°F to 105.4°F.

PATHOLOGY

On biopsy or necropsy, the primary gross lesions are circumscribed to coalescing white, tan or slightly pink irregular nodules or foci of white discoloration ranging from 5 to 30 mm in greatest dimension on the surface and within the parenchyma of spleen, liver, kidneys, lung, mesentery, and lymph nodes.¹ Splenomegaly, renomegaly, hepatomegaly, and ascites have also been noted.

Histologic lesions have been detected in the mesentery/peritoneum, lymph nodes, spleen, kidneys, liver, lung, intestine, pancreas, stomach, brain, and adrenal glands. Other notable lesions include nonsuppurative meningoencephalitis and suppurative or nonsuppurative tubulointerstitial nephritis.¹ Coronavirus antigen was detected in all tissues with lesions, however the staining reaction was most prominent in lymph nodes, splenic lymphoid follicles, and all foci of pyogranulomatous inflammation.¹

CURRENT ASSESSMENT AND VIROLOGY

FSCV has similar gross and histologic lesions to those in cats with FIP. It resembles the "dry form" of FIP with widespread nodular foci on serosal surfaces and within the parenchyma of thoracic and abdominal viscera. There is also nodular enlargement of mesenteric lymph nodes. Clinically, some practitioners have reported effusions in the body cavities resembling the "wet form," but this has not been the predominantly reported or documented finding. Designating "wet" or "dry" forms is somewhat arbitrary as many cats exhibit lesions consistent with both forms during the course of the disease. This is likely the case in ferrets. As more cases are collected, more effusive cases may be documented.

On sequencing, there is slight cross-reactivity in some samples with the FECV-specific primers that may indicate sequence conservation between nucleocapsid genes of FSCV and FECV. Further genomic sequencing of the virus is required. In conclusion, the relatively recent recognition of this disease in pet ferrets suggests a recent mutation or shift in the FECV resulting in the

systemic disease. This is similar to the mutations that occurred in FCOV preceding the development of FIP-1

DISSEMINATED IMMUNOPATHIC MYOSITIS

Disseminated immunopathic myositis (DIM) was not described prior to 2003. It is characterized by a fatal, inflammatory condition of the muscles. Ferrets have typically been between 3 and 24 months of age, with the average age being 10 months. There is no sex predilection and ferrets have been from a variety of breeders.

The clinical presentation is one of rapid onset, characterized by high fever (105–108°F), anorexia, and reluctance to move. There may be variable lymphadenopathy and splenomegaly. Hematology usually shows a neutrophilic leukocytosis. Serum chemistries may show an elevated AST, hyperglycemia, and hypoalbuminemia. Most ferrets have some degree of dehydration and are losing weight and condition. Some ferrets with DIM also show diarrhea, mild serous nasal discharge, and have increased heart and respiratory rates. Radiology and ultrasonography usually show no abnormalities. Biopsies of skeletal muscle from the hind leg or lumbar region, lymph nodes and/or any masses may be useful for antemortem diagnosis and prognosis. If necropsy tissues are submitted, esophagus, heart, skeletal muscle (several sites), diaphragm, lymph nodes, spleen, bone marrow are most definitive, although full tissue submission is preferred.

Many therapies have been attempted in efforts to reduce the fever and inflammation associated with this disease, but rarely has there been recovery. Antibiotic therapy including penicillins, cephalosporins, fluoroquinolones, doxycycline, clarithromycin, azithromycin, trimethoprim-sulfa, aminoglycosides, metronidazole, and chloramphenicol has been unsuccessful. Treatment with steroidal and nonsteroidal anti-inflammatory drugs (NSAIDs) also has had little effect. Other drugs including antifungal and antiviral agents have been ineffective in controlling signs of DIM. Interferon-alpha at a dose of 600 IU/day has been shown to reduce the fever in a few cases temporarily. Cyclophosphamide has also been without much success. As most ferrets require fluid therapy, nutritional supplementation and analgesia as the disease progresses, many owners elect euthanasia following the biopsy diagnosis. To date, the author has not successfully treated this: all patients succumbed.

PATHOLOGY

Gross lesions include atrophy of skeletal muscle throughout the body including the esophagus (described as red and white mottling, dilatation). Histologically there is moderate to severe suppurative to pyogranulomatous inflammation of skeletal muscle and fascia of the esophagus, heart, limbs, body wall, head and lumbar regions. There is myeloid hyperplasia of the spleen and/or bone marrow. On electron microscopy lesions include mitochondrial swelling, intracellular edema, disruption of myofibrils and Z bands.³

At this time, the etiology of DIM is unknown. No pathogen has been isolated in any of the confirmed cases by bacterial or viral cultures, EM, immunohistochemistry, or polymerase chain reaction testing for a wide variety of known pathogens. One vaccine from one manufacturer is the only known commonality. This vaccine is no longer available, and so it is unknown if we will continue to see this syndrome. We have not had any cases presented in the past year. In an experimental trial using the canine castration vaccine, this myofasciitis syndrome was reproduced in the entire group, suggesting that it is an immunological response to an initial inflammatory stimulation.

APLASTIC ANEMIA/BONE MARROW

This condition has been seen repeatedly in ferrets across the country. Cases are being tabulated, but so far, the only discernible pattern is that the ferrets are under 18 months of age. They are presented due to lethargy and anorexia, but upon physical examination are found to have pale to white mucus membranes. Some have moderate splenomegaly, but other physical parameters appear normal. Packed cell volumes are less than 10%. Bone marrow aspirations have shown erythrocytic aplasia. These ferrets tend to have normal white blood cell counts, and serum chemistries are often normal. Although transfusions are done, erythropoietin therapy is usually ineffective. High doses of corticosteroid have been tried to try an rule out an immune-mediated disease: this has also seemed ineffective. Etiology is unknown, but collection of case information and full necropsy work needs to be done.

ACUTE HEMORRHAGING SYNDROME

This syndrome has manifested within the past year and seems to occur mainly in recently shipped ferrets or ones recently placed in pet stores. One of the major pet store chains alerted veterinarians to it in their August newsletter (Edling T, PetCo Newsletter) These young kits have acute hemorrhage, often first as epistaxis, and from oral ulceration. Hemorrhages can also be seen from the rectum, and petechiation may appear on the skin. Hemorrhage within the abdominal cavity has also been seen. Immediate therapy with parenteral vitamin K and supportive care appears to have stopped the hemorrhaging if caught early, but many literally bleed out no matter what treatment is attempted. If possible, blood can be drawn for a coagulation profile antemortem: it is speculated that this may be a hemophilia disease. Normal coagulation parameters on ferrets need to be collected and then compared. If you encounter this, please collect blood for a coagulation profile, attempt therapy, and contact Dr. Drury Reavill, who is coordinating the pathology work.

AMINO ACID METABOLISM ABNORMALITIES

Two conditions are being found in ferrets that appear to be genetic metabolism pathway abnormalities. One is cysteine metabolism, which results in cysteine urolithiasis. Ferrets that have shown this condition have all been on novel protein diets. L-carnitine metabolism

abnormality is being linked to skeletal muscle weakness in older ferrets, particularly in the hind legs. Supplementation with L-carnitine has ameliorated the most severe symptoms, but further characterization of this needs to be done. Dr. Michelle Hawkins is working on various genetic disease issues in ferrets. If you encounter urolithiasis in ferrets, stone analysis can be performed at the University of California, Davis. Contact Dr. Hawkins concerning the case.

CONCLUSION

A number of emerging diseases in ferrets need to be researched prior to effective treatments or preventive measures can be accomplished. Practitioners need to

share case information particularly with pathologists and investigators if we are to solve these clinical dilemmas.

REFERENCES

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