DISSEMINATED IDIOPATHIC MYOSITIS (DIM) IN FERRETS

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Disseminated idiopathic myofasciitis (DIM) is disease that affects pet ferrets (Mustela putorius furo). DIM is a severe inflammatory condition that affects primarily muscles and surrounding connective tissues. There have been hundreds of suspected and confirmed cases since the disease was first identified in 2003. For several years the disease was considered to be a hopeless, fatal disease in ferrets, but now we have a fairly effective treatment protocol and many long-term survivors.

Signalment and History:
DIM generally affects ferrets between 5 months and 2 years of age, although the disease has been diagnosed in ferrets as old as 4 years. Both male and female ferrets (most neutered at an early age) are susceptible to DIM. There is no apparent association between the disease and diet, environment, or geographical location of ferrets with DIM. Almost all of the ferrets diagnosed or suspected to have DIM have come from large breeding facilities, but a few have been from private breeders.

Vaccine histories were evaluated from many confirmed cases. All confirmed cases had received at least one distemper vaccination. Some DIM ferrets had received the recommended series of distemper vaccinations, but some had only been inoculated with one canine distemper vaccination between 4 and 7 weeks of age at the breeding facility. It is important to note that some ferret owners have the misconception that young ferrets have been fully vaccinated against canine distemper before being shipped to a pet store. Canine distemper is usually a fatal disease in unprotected ferrets, so ferrets should be vaccinated against canine distemper with an appropriate canine distemper vaccine. A distemper titer may be considered in older ferrets that have received previous distemper vaccinations.

Clinical Signs:
The onset of clinical signs for DIM is usually fairly fast, often followed by a rapid decline over a period of 12 to 48 hours. Affected ferrets usually have multiple, concurrent clinical signs, with a high fever (104-108 F), severe lethargy, general weakness, and dehydration being the most common initial signs. Most affected ferrets are depressed but aware of their surrounding environment. Other clinical signs observed in ferrets during the onset of DIM include decreased appetite, enlarged lymph nodes or masses under the skin and abnormal stools (can be green, dark, mucoid, diarrhea). Some ferrets will refuse to eat their kibble, but will eat soft food such as canned food or duck soup. Often ferrets will become sensitive, especially in the back end, showing signs of pain when touched and are often reluctant to move. Many ferrets with DIM have an elevated heart rate and many acquire heart murmurs as the disease progresses. Other clinical signs that can be observed in ferrets with DIM include clear discharge from the nose, labored breathing, coughing, discharge from the eyes, pale gums, tooth grinding, and occasionally fluid accumulation under the skin or seizures. Some ferrets have tiny, orangish dots on their skin on their trunk and face. Ferrets untreated or treated with ineffective drugs usually continue to progressively decline until they die or are humanely euthanized. Over the last 10 years, many ferrets definitively diagnosed with DIM or those strongly suspected to have DIM that have been treated with the current treatment protocol have recovered from the disease.

Diagnostic Results:
Ferrets with DIM may initially have a white blood cell count that is in the normal range, but it often increases within a few weeks of the onset of the disease. Many DIM ferrets have a moderate to marked increase in mature neutrophils, occasionally with a left shift. The white blood cell count is less than 50,000/ul in most DIM cases (normal reference range is 2,500-8,000/ul). Sometimes immature white blood cells are observed and neutrophils are often slightly to moderately toxic in ferrets with DIM. Mild to moderate anemia (decreased red blood cells) is often observed in DIM ferrets.

Commonly observed changes in serum chemistry values in ferrets with DIM include a mild increase in glucose and a decrease in albumin (blood protein). Liver values are usually within normal limits, but one liver value (ALT) can be mildly to moderately increased. Interestingly, creatine kinase (enzyme from muscle), which is typically elevated with severe inflammation and muscle tissue necrosis, is NOT elevated in ferrets with DIM. It is thought that this is because although there is severe inflammation within the muscle bundles and areas between muscles, there is usually minimal muscle necrosis.

Radiographs and ultrasounds performed on ferrets with DIM often show an enlarged spleen and/or enlarged abdominal lymph nodes, but these are nonspecific findings. Bacterial cultures done on various affected tissues have been negative in ferrets with DIM. Interestingly, the urinalysis results from several cases studied have shown a slightly elevated urine pH

of 7-8 (normal range is 5.5-6.5).

Pathologic Findings:

Biopsies of enlarged lymph nodes and muscle tissue from ferrets with DIM reveal severe, widespread inflammation, often with suppurative (pus) changes. The inflammation has a multi-focal distribution, so some ferrets suspected to have DIM may have negative muscle biopsies. Obtaining more than one small biopsy will increase the changes of observing the disease if it is present.

Postmortem findings from DIM ferrets that died or were euthanized show severe inflammation of muscle tissue (skeletal, cardiac, and some smooth muscle). The esophagus is often particularly affected and marked atrophy of diaphragm and skeletal muscle can be observed in advanced cases. Inflammation often extends into surrounding fatty tissue and muscle atrophy and fibrosis may be observed in ferrets with chronic disease. All muscle groups appear to be affected in ferrets with DIM and it is likely that the clinic signs observed are a result of the pain and atrophy that accompany this condition.

Diagnosis:

A presumptive diagnosis of DIM can be made based on a ferret's clinical signs and signalment. A definitive diagnosis can best be made by obtaining surgical biopsies of external muscle tissue. However, some ferrets are too weak to undergo anesthesia and surgery, some owners have financial constraints and cannot afford biopsies, and sometimes owners prefer to treat their ferret presumptively for DIM.

Treatment:

One consistent characteristic of ferrets with DIM has been a general lack of response to treatment and a high mortality rate. Treatment with various antibiotics and other medications such as glucocorticoids, non-steroidal anti-inflammatory drugs, antipyretics, pain medications, interferon and cyclosporine have been unsuccessful in treating DIM patients. Acupuncture was helpful and gave pain relief to one ferret with DIM.

Since 2006, many confirmed and suspected cases of ferrets with DIM have improved and recovered from DIM. The combination of cyclophosphamide (chemotherapy drug), prednisolone (steroid), and chloramphenicol (antibiotic) have been used to successfully cure many DIM ferrets. As prednisolone and antibiotics, including chloramphenicol, have been used unsuccessfully to treat DIM ferrets, this author believes that cyclophosphamide is the key drug in treating the disease.

Published Treatment Protocol:

Drug	Suggested Dose	Potential Side Effects
Prednisolone	1 mg/kg orally every 12 hours for 3 months, then once a day until recovery has been achieved (must wean off prednisolone)	GI ulcers, muscle wasting, elevated liver enzymes, abdominal fat deposition, increased drinking, urinating, and increased appetite
Cyclophosphamide	10 mg/kg on day 1, day 14, then every 4 weeks for 3 months or until recovery has been achieved	Affects on the bone marrow, hemorrhagic cystitis, GI toxicity
Chloramphenicol	50 mg/kg by mouth twice a day for 6-8 weeks	Bone marrow suppression, GI signs

Supportive Care is important!

Ferrets with DIM often have a poor appetite. Because the esophagus is a primary target in ferrets with DIM, it may be painful to eat (especially crunchy food). Supplemental feedings of a high quality canned cat food or other food that can be syringe fed (e.g. Duck soup or Carnivore Care) are often needed. Prescription foods can be obtained at a vet office, but many pet stores carry high quality, meat-based foods. The food can be mixed with a little water, pureed and served warm several times throughout the day. Food with peas (peas, pea flour, pea fiber, etc.) should be avoided! Supplemental subcutaneous (under the skin) fluids are often needed to help with dehydration. Some DIM ferrets are anemic and a low dose of a multivitamin with iron may be helpful.

Note:

1. Prednisolone can be made up as a "bitter-free" oral suspension that is more palatable than some human commercial formulations. 5 mg/ml is a good concentration to use as it is easy to measure and administer.
2. Subcutaneous fluids should be administered immediately prior to administration of cyclophosphamide to help reduce potential for hemorrhagic cystitis.

3. Cyclophosphamide can be given via a subcutaneous injection. Oral cyclophosphamide may be given, but it is not palatable to ferrets and partial tablets should not be given as the drug is not evenly distributed throughout the tablet. Some compounding pharmacies are able to split a bottle of cyclophosphamide powder into smaller bottles (e.g. 20 mg vials) so that each dose can be reconstituted immediately before use. Note: Cyclophosphamide powder (injectable) is only good for 6 days in the refrigerator (or 24 hrs at room temperature) once it is reconstituted.
4. It is best to have the ferret's complete blood count checked prior to each cyclophosphamide treatment.
5. Chloramphenicol palmitate oral suspension can be made at a compounding pharmacy.
Based on the response of DIM ferrets to the recommended treatment protocol over the last several years, this author has

Optional Treatment Protocol:

1. **Cyclophosphamide:**

* 10 mg/kg to be given on day 1, day 14, and then every 2-4 weeks as needed

* It is important to note that many ferrets begin to decline clinically as they are approaching the need for another dose of cyclophosphamide.

* The CBC should be monitored while a ferret is receiving cyclophosphamide treatments

2. **Prednisolone:** (5 mg/ml; bitter-free oral suspension):

* 1 mg/kg by mouth once a day for 2-4 weeks, then 0.5 mg/kg once a day for an additional 2-4 weeks (longer if needed). Again, a ferret should be weaned off the prednisolone slowly when the medication is being discontinued.

new treatment recommendations.

Prognosis:

The prognosis for ferrets with DIM that are treated appropriately is relatively good. We now have many suspected and confirmed cases that have responded to therapy and have become long term survivors. The treatment appears to be most successful when the medications are started as early on in the disease process as possible, but a number of ferrets have recovered even when the medications have not been started right away. DIM is not a common disease and it can sometimes take awhile for a ferret's illness to be recognized as being DIM. Some ferrets that have been sick for too long may not respond to treatment. Not all ferrets with DIM respond to treatment, but many of them do.

Recommendations:

Ferrets suspected of having DIM should have a thorough physical examination and diagnostic tests, including a comprehensive blood panel, urinalysis, and preferably radiographs. When a ferret's signalment and clinical signs are consistent with those of DIM and diagnostic test results are consistent with those found in ferrets with DIM, then surgical biopsies or presumptive treatment of DIM should be strongly considered. Ferrets confirmed to have DIM or ferrets strongly suspected of having DIM should receive aggressive supportive care in addition to medications listed in the treatment protocol. DIM is considered fatal in ferrets that are not treated for the disease, but ferrets with DIM that are treated appropriately have a reasonable chance of recovery.

Summary:

DIM is a severe inflammatory disease in ferrets that affects primarily skeletal, smooth, and cardiac muscles. The disease affects both male and female ferrets and is most common in ferrets less than 18 months of age. DIM has distinct clinical features that can help with a presumed diagnosis, but the only way to get a definitive diagnosis in a living ferret is to obtain muscle biopsies of skeletal muscle and have the samples sent to a pathologist. If surgical biopsies aren't a reasonable option, then presumptive treatment is often warranted in suspected cases. Although the pathogenesis of DIM is still poorly understood, it is thought that DIM may be an acquired vaccine-associated, immune-mediated disease. DIM is uncommon and ferrets should continue to be properly vaccinated. Although DIM has been previously considered to have a high mortality rate, we now have a fairly effective treatment protocol and many long-term survivors.

References:

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Veterinarians or ferret owners who have questions or concerns about a suspected or confirmed DIM ferret may contact Dr. Ramsell directly at:

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