Published in final edited form as:

J Am Vet Med Assoc. 2013 January 1; 242(1): 43–45. doi:10.2460/javma.242.1.43.

Pathology in Practice

Catherine M. Pfent, DVM, MS, Joanne Mansell, DVM, DACVP, Roy R. Pool, DVM, PhD, and Marilyn E. Mitchell, DVM

Department of Pathobiology, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843 (Pfent, Mansell, Pool); and the Small Animal Wellness Center, 1400 N Locust St, Denton, TX 76201 (Mitchell)

History

A 634-g (1.4-lb) 14-month-old castrated male ferret was evaluated because of lethargy, decreased appetite, and a 2-cm-diameter nodular mass in the inguinal area. The ferret was anesthetized via IM administration of buprenorphine hydrochloride and inhalation of isoflurane and oxygen, and a punch biopsy specimen of the mass was obtained. Sections of the biopsy specimen were stained with H&E or Gram stain for bacteria. The results of the histologic examination were indicative of pyogranulomatous steatitis; a few intralesional cocci were present in the mass tissue. Clarithromycin was administered orally twice daily to the ferret, and the mass decreased in size by 90% over 3 to 4 weeks; however, the ferret's lethargy progressed and swelling developed around the neck.

Clinical and Gross Findings

One month after the initial evaluation, the ferret was examined again. The ferret was pyrexia (41.06°C [105.9°F]) and anorexic; it was reluctant to move and had weak withdrawal reflexes, bruxism, signs of pain on palpation of the abdomen, and labored breathing. A CBC and serum biochemical analysis revealed marked leukocytosis with neutrophilia and an appropriate left shift, mild to moderate anemia, mild hyperglycemia, moderate hypokalemia, moderate hypoalbuminemia, and mild hyperglobulinemia. The ferret failed to respond to treatment with enrofloxacin, clindamycin, furosemide, famotidine, and buprenorphine. The ferret's quality of life continued to decline, and it was euthanized.

The gross findings at necropsy included diffuse pulmonary edema, cardiomegaly, bilateral renomegaly, hepatomegaly, small pale areas in the heart and skeletal muscles, and marked generalized skeletal muscle atrophy. The entire esophagus was dilated and flaccid, and the esophageal wall was thickened (Figure 1). The spleen was markedly enlarged (weight, 20 g [approx 3% of the ferret's body weight; normal spleen weight is 0.5% to 1.3% of a ferret's body weight]), had rounded edges, and was soft, pale, and mottled pink and tan.

Histopathologic Findings

Tissue samples from the esophagus, limb muscles, eyes, diaphragm, tongue, lungs, heart, intestines, and spleen were routinely processed for histologic examination. Histologic examination of the esophagus revealed severe, transmural, neutrophilic, chronic-active esophagitis, and periesophagitis; smooth muscle fibers were atrophied and infiltrated by large numbers of degenerate and nondegenerate neutrophils with fewer lymphocytes, plasma cells, and macrophages (Figure 2). Some areas of the esophageal wall contained fibrosis, edema, and necrosis. Similar inflammatory cells were detected within the striated muscles of the limbs, eyes, diaphragm, tongue, and heart and within the smooth muscle of the bronchi and bronchioles of the lungs, trachea, great vessels of the heart, and intestines. The spleen was pale and swollen because of large numbers of myeloid precursor cells and megakaryocytes (Figure 3).

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: severe, chronic-active, transmural, neutrophilic esophagitis and periesophagitis with mild myofiber atrophy and marked, diffuse extramedullary myelopoiesis of the spleen.

Case summary: myofasciitis in a ferret.

Comments

Disseminated idiopathic myofasciitis (DIM), also known as disseminated idiopathic myositis, polymyositis, or simply myofasciitis, was first identified in ferrets in 2003.^{1–3} It is believed to be an immune-mediated disease triggered by vaccine or drug injections.⁴ Disseminated idiopathic myofasciitis typically affects young domestic ferrets < 2 years of age, and most affected animals die. Clinical signs include pyrexia, lethargy, recumbency, ataxia, posterior paresis, signs of pain during movement, bruxism, anorexia, or difficulty swallowing or drinking. Affected ferrets often have mild to moderate anemia, mild to marked leukocytosis with mature neutrophilia, mildly to moderately high serum alanine aminotransferase activity, mild hyperglycemia, and mild hypoalbuminemia. Serum aspartate aminotransferase and creatine kinase activities are rarely high, despite DIM being a disease of the muscles, because the inflammation separates and atrophies the muscle fibers rather than causes cellular damage. Given that it is too painful for affected ferrets to eat, it is logical to assume anorexia would result in hypoglycemia. However, ferrets with myofasciitis are often hyperglycemic, which is often confusing to veterinarians. Because of the pain associated with DIM, affected ferrets are unable to move normally, which could be easily misinterpreted to indicate neurologic disease.

The gross lesions of DIM include dilation of the esophagus; mild (acute) to severe (chronic) atrophy of skeletal muscles; mild atrophy of the tongue; white streaks in the heart, diaphragm, and intercostal muscles; and splenomegaly.² Histologically, the most consistent lesion is neutrophilic to pyogranulomatous inflammation of skeletal, cardiac, and smooth muscles throughout the body. Because of the large number of neutrophils, the character of the inflammation may suggest a bacterial infection and therefore be misdiagnosed by

pathologists unaware of this condition. Most ferrets with DIM have a pale and markedly swollen spleen attributable to myeloid hyperplasia; the spleen is more diffusely pale as a result of myeloid hyperplasia than it appears as a result of enlargement due to a combination of congestion and extramedullary hematopoiesis. Splenomegaly is a common lesion in ferrets and is often due to congestion, extramedullary hematopoiesis, lymphoid hyperplasia, or neoplasia; however, most enlarged spleens in ferrets are red, whereas the spleens in ferrets with DIM are often pale tan.

In a clinical setting, DIM can be diagnosed on an antemortem basis by collection and histologic examination of multiple skeletal muscle biopsy samples. The diagnosis is confirmed when the histopathologic findings are consistent with neutrophilic and pyogranulomatous myositis and the ferret has neutrophilia along with other clinical signs associated with DIM. The prognosis for ferrets with DIM is grave. A small number of ferrets have been successfully treated with a combination of prednisolone, cyclophosphamide, and chloramphenicol.³

A tentative postmortem diagnosis of myofasciitis can be made for a ferret with a compatible clinical history in conjunction with appropriate necropsy findings. One consistent and striking necropsy finding is a dilated and thickened esophagus. The diaphragm from affected ferrets is often so thin that one can read printing through it (Figure 4). In cases of suspected DIM, multiple tissue samples, especially samples of esophagus, tongue, heart, spleen, and skeletal muscle tissues, should be fixed in neutral-buffered 10% formalin and sent for histologic examination. Histologic examination is necessary to identify the expected pattern of inflammation involving the muscle and fascia, especially in the esophagus and other muscular tissues. Multiple tissue samples may be frozen and stored in case the diagnosis of DIM is not confirmed and additional diagnostic tests are required.

When DIM in ferrets was first described, administration of a now discontinued canine distemper vaccine^a was the single common entity among all the affected animals.^{1,2} Disseminated idiopathic myofasciitis has also developed in ferrets that were administered an experimental castration drug.⁴ The number of reported cases of ferrets with myofasciitis peaked in 2004 and 2005³ and has since declined, which coincides with the discontinuation of the aforementioned canine distemper vaccine^a in 2006, but a direct causative role of vaccination and the development of myofasciitis is yet to be determined. The case described in the present report highlights that ferrets may still develop DIM, and it is possible that other vaccines or injectable drugs may potentiate the onset of the disease. One of the authors of the present report (CMP) has confirmed a diagnosis of DIM for 6 ferrets in the interval since the aforementioned canine distemper vaccine^a became unavailable, and it was verified that those ferrets had not received that vaccine. The breeder of the ferret of this report had been routinely administering 1 of 2 available canine distemper vaccines^{b,c} at the time the ferret was housed within the breeder's facility but did not record which vaccines were administered to which ferrets. The ferret received a single canine distemper vaccination

^aFervac-D, United Vaccines Inc, Fitchburg, Wis.

^bGalaxy D, Schering-Plough, Kenilworth, NJ.

^cPurevax, Merial, Duluth, Ga.

during its lifetime, which was administered by the breeder 1 year before the onset of clinical signs. Other injections administered to the ferret included an IM injection of buprenorphine during the biopsy of the inguinal mass. It has been documented that some ferrets with DIM have subcutaneous nodules; however, it could not be determined whether the ferret was in the early stages of DIM at the time of the biopsy procedure or the stress associated with anesthesia and the procedure or the buprenorphine injection activated the onset of DIM. Although rare, DIM should remain a differential diagnosis in febrile ferrets < 2 years of age that have signs of generalized pain.

References

1. Garner MM, Ramsell K. Myofasciitis: an emerging fatal disease of the domestic ferret. *Exot DVM*. 2006; 8:23–25.
2. Garner MM, Ramsell K, Schoemaker NJ, et al. Myofasciitis in the domestic ferret. *Vet Pathol*. 2007; 44:25–38. [PubMed: 17197621]
3. Ramsell KD, Garner MM. Disseminated idiopathic myofasciitis in ferrets. *Vet Clin Exot Anim*. 2010; 13:561–575.
4. Schoemaker NJ, Lumeij JT, Rijnberk A. Current and future alternatives to surgical neutering in ferrets to prevent hyperadrenocorticism. *Vet Med*. 2005; 100:484–496.

Figure 1.

Photographs of longitudinal and cross-sectional views of the formalin-fixed esophagus (A [bottom row]) and the unfixed spleen (B) from a 15-month-old castrated male ferret that was evaluated because of pyrexia, anorexia, and reluctance to move. An unaffected formalin-fixed esophagus from a ferret that was euthanized because of lymphoma and insulinoma (A [top row]) has been provided for comparison. In both panels, bar = 1 cm.

Figure 2.

Photomicrograph of a section of the esophagus from the affected ferret in Figure 1. Notice the infiltration of numerous degenerate and nondegenerate neutrophils and mild myofiber atrophy in the esophageal wall. H&E stain; bar = 50 μ m. Inset—Subgross photograph of the esophagus. Notice the severe transmural esophagitis and periesophagitis. The box outlines the area included in the main image. H&E stain.

Figure 3. Photomicrograph of a section of the spleen from the affected ferret in Figure 1. Notice the marked diffuse extramedullary myelopoiesis. H&E stain; bar = 50 μm.

Figure 4. Photograph of the diaphragm from another ferret that was euthanized because of myofasciitis. The muscle is very thin; when placed over handwriting on a piece of paper, one can see the letters through the muscle.