

Biliary Coccidiosis in a Ferret (*Mustela putorius furo*)

B. H. WILLIAMS, M. J. CHIMES, AND C. H. GARDINER

Abstract. This report documents the first case of biliary coccidiosis in the ferret. Multiple life stages of a coccidian parasite, including meronts, gametocytes, and oocysts were present in the epithelium of hepatic bile ducts and the gallbladder. Based on morphologic characteristics, the organisms were identified as *Eimeria* sp., most likely *E. furonis*.

Key words: Ferret; coccidia; Biliary tree; *Eimeria*.

An 9-week-old male research colony ferret was presented to a veterinarian for evaluation of emaciation and poor appetite. The ferret had appeared clinically normal when received from a commercial vendor 3 weeks earlier. Upon examination, abdominal distention and slight icterus were noted. Fecal flotation and direct smear were negative for parasites. Addition of a high calorie nutritional supplement to the ration (Nutrical®, Evsco, Buena, NJ) was recommended.

One week later, after seeing no improvement, a blood sample was collected and the animal was euthanatized. Clinicopathologic abnormalities included marked elevations of alkaline phosphatase (3533 IU/liter), total bilirubin (4.8 mg/dl), and a moderately elevated alanine aminotransferase (853 IU/dl). Additionally, the animal was azotemic (BUN = 62 mg/dl), hyperphosphatemic (9.3 mg/dl), hypoproteinemic (5.1 g/dl), and mildly hypoalbuminemic (2.6 g/dl). A complete blood count revealed marked neutrophilic leukocytosis (45,000/ml) with a regenerative left shift (73% neutrophils, 4% bands) and macrocytic normochromic anemia (HCT 23.7%, RBC 4.06×10^6 , MCV = 58.4 fl, MCHC = 35.0 g/dl). At necropsy, the liver was grossly enlarged and pale. Bile ducts appeared enlarged and firm, and the gallbladder wall was thickened. Tissue samples from the liver, gallbladder, and intestine were collected, fixed in 10% neutral-buffered formalin, and submitted for microscopic examination.

Tissues were embedded in paraffin, sectioned at 6 μ m, and stained with hematoxylin and eosin, Brown-Brenn and Brown-Hopps tissue Gram stains, periodic acid-Schiff (PAS), Gomori's methenamine silver, and Ziehl-Nielsen's acid fast stain. Additionally, sections of formalin-fixed tissue were post-fixed in osmium tetroxide, embedded in epoxy resin, thin-sectioned, and stained with uranyl acetate and lead citrate for transmission electron microscopy.

Microscopic examination of the gallbladder wall revealed marked thickening up to eight times normal (4 mm). The mucosa was thickened to 3 mm by proliferation of cystic glands separated by a moderate amount of mature fibrous connective tissue and numerous lymphocytes, plasma cells, macrophages, and neutrophils. Moderate numbers of similar inflammatory cells and sloughed epithelial cells were present in the gallbladder lumen. Within the liver, interlobular bile ducts were reduplicated and surrounded by abundant fibrous connective tissue. Portal areas were further expanded by moderate numbers of lymphocytes and plasma cells and lesser numbers of neutrophils and macrophages, which extended into the surrounding hepatic sinusoids (Fig. 1). Dilated bile

ducts occasionally contained proliferating mucosal epithelial cells that formed papillary and micropapillary projections. Moderate numbers of lymphocytes and plasma cells traversed the duct epithelium into the lumen, where they were admixed with sloughed epithelial cells, low numbers of degenerated neutrophils, and abundant cellular debris.

Coccidian meronts were present within approximately 20% of intact gallbladder and biliary epithelial cells, as well as in sloughed epithelial cells at both sites, and rarely found free in the lumens. All stages of development were present (Fig. 2). Meronts measured $10.8-13 \times 8.9-9.3 \mu$ m. Most meronts contained merozoites; both meronts and merozoites were PAS-negative. Meronts contained up to 16 merozoites, which were seen both randomly arranged within the mature meront and budding from a residual body. Longitudinally cut merozoites measured $5.6-6.4 \times 1.5-2.0 \mu$ m. Merozoites were arranged randomly within epithelial cells, often head to tail; they were curved at the broader posterior end, and pointed at the narrower anterior end. Nuclei were present at or near the curved posterior end. Oocysts were seen within epithelial cells in the gallbladder and hepatic bile ducts, and also free in the lumen at these sites. They were oval to spherical and measured $12.5 \times 12.0 \mu$ m.

Ultrastructurally, merozoites contained a double-layered pellicle, a prominent conoid, a few rhoptries, and numerous micronemes located anterior to the nucleus (Fig. 3).

Coccidia that have previously been reported to infect mustelids include the genera *Toxoplasma*, *Isospora*, and *Eimeria*.^{3,8-10,12,14,15} Four species of coccidia have been reported in the ferret. *Isospora laidlawi* was described in the original manuscript by Hoare in 1927,⁸ but has not been reported since. *Eimeria ictidea* has been reported as infecting the small intestine selectively at the villar tips, whereas *Eimeria furonis* has been reported to infect both the small intestine and rectum, and along the entire length of the villus.^{3,8} *Toxoplasma gondii* has been reported twice in ferrets; however, infection of biliary epithelium was not documented in either report.^{10,14} Additionally, in this case, the presence of gametocytes within biliary epithelium is not consistent with the life cycle of *T. gondii*, in which sexual stages are found only in the intestine epithelium of felids, the natural host.

The organisms seen within epithelial cells of the biliary system of this ferret closely resemble *E. furonis* as described by Hoare in 1927.⁸ Although definitive generic designation cannot be made in histologic section, we are assured that the organism is *Eimeria* sp. and that the species is most likely *E. furonis*. *E. furonis* is described as having oocysts that

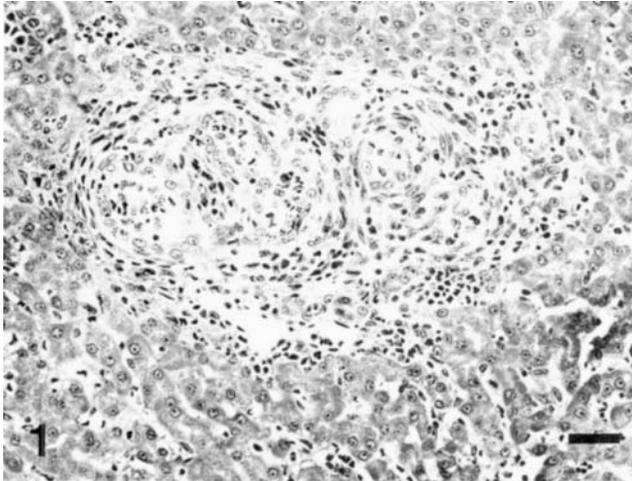


Fig. 1. Liver; ferret. Portal area is expanded by pronounced interlobular biliary duct reduplication, fibrosis, and lymphoplasmacytic inflammation. HE. Bar = 30 μ m.

measure 12.8 \times 12.0 μ m and schizonts with 13 merozoites.^{8,9} Another closely related species, *E. ictidea*, is described in the ferret; however, the dimensions of its oocyst are 23 \times 17.5 μ m.⁸

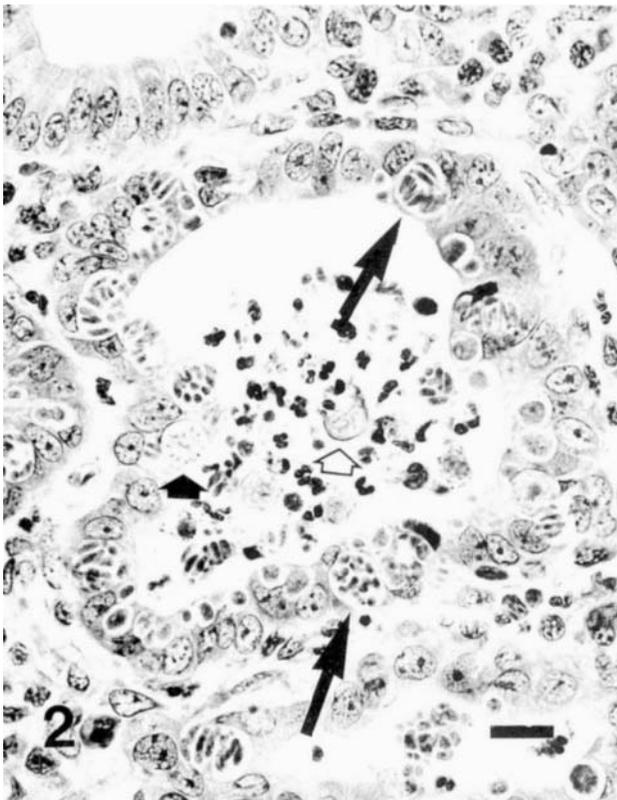


Fig. 2. Gallbladder; ferret. Several life cycle stages are present within the epithelium including meronts (arrows), microgametocytes (arrowhead), and an oocyst within the lumen (hollow arrowhead). HE. Bar = 15 μ m.

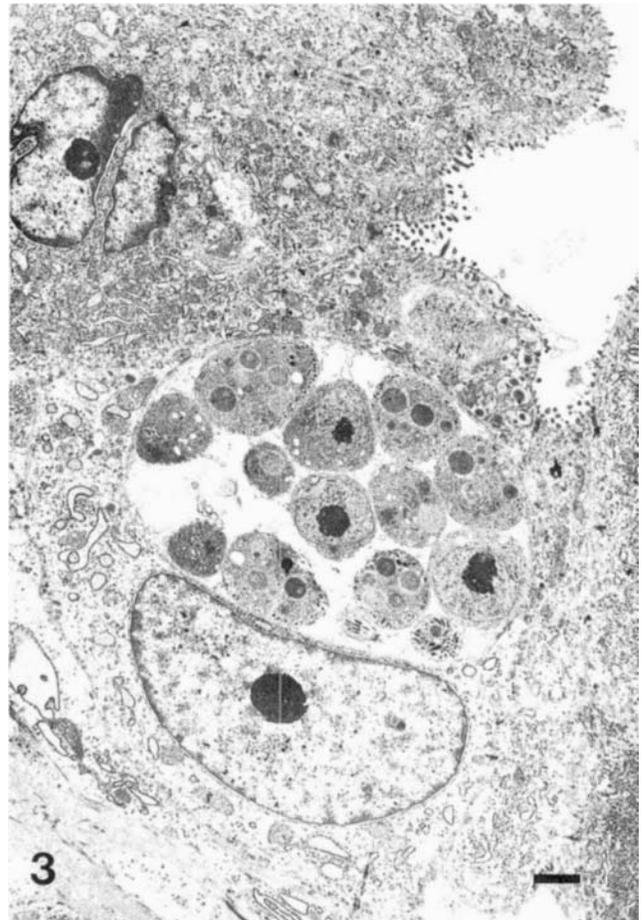


Fig. 3. Liver; ferret. Electron micrograph of a coccidian meront within a biliary epithelial cell. Conoid processes, rhoptries, and numerous micronemes are visible within several merozoites. Bar = 1.5 μ m.

Eimeria furonis has rarely caused clinical disease in the ferret. It has been reported in both the domestic ferret (*Mustela putorius furo*)⁸ and the black-footed ferret (*Mustela nigripes*);¹² however, clinical disease has not been associated with *E. furonis* in black-footed ferrets. A recent review article states that *Isospora* sp. oocytes are commonly shed by ferrets 6 to 16 weeks of age and are the same species that commonly affects puppies and kittens, but the species of this parasite is not identified.² In several cases of coccidiosis in domestic and black-footed ferrets, simultaneous infection with canine distemper virus was found.^{8,15}

Biliary coccidiosis is an uncommon finding in animals. This case represents the first report of biliary coccidiosis in the domestic ferret. Other species in which biliary eimeriasis has been reported include rabbits (*E. steidae*),¹ mink (*E. hiepei*),⁵ and ophidian snakes (*E. bitis*).⁷ Unidentified species of coccidia with features of the family Eimeridae have been reported in the biliary epithelium of a dog,¹¹ a cat,¹³ a goat,⁶ and a calf.⁴ The clinical pathology in this ferret shares several features in common with *E. steidae* infection in the rabbit:¹ mature neutrophilia, hypoalbuminemia, hyperbilirubinuria,

and mild elevation of alanine aminotransferase. Several histopathologic features of this case also closely resemble similar syndromes in rabbits¹ and mink:⁵ restriction of coccidians to the hepatobiliary epithelium and subacute cholangiohepatitis with marked epithelial hyperplasia, bile duct reduplication, and portal fibrosis.

Acknowledgements

We would like to thank Ms. Robin-Anne V. Ferris, M.F.S., and Mr. John H. Jenkins of the Armed Forces Institute of Pathology for excellent photographic and electron microscopic support, respectively. The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

References

- 1 Barriga, A: Pathophysiology of hepatic coccidiosis in rabbits. *Vet Parasitol* **8**:201–210, 1981
- 2 Bell JA: Parasites of domesticated pet ferrets. *Comp Clin Educ Pract Vet* **16**:617–620, 1994
- 3 Blankenship-Paris TL, Chang J, Bagnell CR: Enteric coccidiosis in a ferret. *Lab Anim Sci* **43**(4):361–363, 1993
- 4 Collins JE, Dubey JP, Rossow KD: Hepatic coccidiosis in a calf. *Vet Pathol* **25**:98–100, 1988
- 5 Davis CL, Chow TL, Gorham JR: Hepatic coccidiosis in mink. *Vet Med* **48**(9):371–375, 1953
- 6 Dubey JP: Coccidiosis in the gallbladder of a goat. *Proc Helminthol Soc Wash* **53**(2):277–281, 1986
- 7 Fantham HB, Porter A: The endoparasites of some North American snakes and their effects on the Ophidia. *Proc Zool Soc Lond* **123**:867–898, 1953
- 8 Hoare CA: On the coccidia of the ferret. *Ann Trop Med Parasitol* **21**:313–319, 1927
- 9 Hoare CA: The endogenous development of the coccidia of the ferret, and the histopathological reaction of the infected intestinal villi. *Ann Trop Med Parasitol* **29**:111–122, 1935
- 10 Lainson R: The demonstration of *Toxoplasma* in animals, with particular reference to members of the Mustelidae. *Trans R Soc Trop Med Hyg* **51**:111–117, 1957
- 11 Lipscomb TP, Dubey JP, Pletcher JM, Altman NH: Intrahepatic biliary coccidiosis in a dog. *Vet Pathol* **26**:343–345, 1989
- 12 Jolley WR, Kingston N, Williams ES, Lynn C: Coccidia, *Giardia* sp., and a physalopteran nematode parasite from black-footed ferrets (*Mustela nigripes*) in Wyoming. *J Helminthol Soc Wash* **61**(1):89–94, 1994
- 13 Neufeld JL, Brandt RW: Cholangiohepatitis in a cat associated with a coccidia-like organism. *Can Vet J* **15**(5):156–159, 1974
- 14 Thornton RN, Cook TG: A congenital *Toxoplasma*-like disease in ferrets (*Mustela putorius furo*). *N Z Vet J* **34**:31–33, 1986
- 15 Williams ES, Thorne ET, Appel MJG, Belitsky DW: Canine distemper in black footed ferrets (*Mustela nigripes*) from Wyoming. *J Wildl Dis* **24**(3):385–394, 1988

Vet Pathol **33**:439–441 (1996)

Adenocarcinoma of the Hepatopancreatic Ampulla in a Domestic Cat

V. L. HAINES, P. R. BROWN, R. H. HRUBAN, AND D. L. HUSO

Abstract. A 13-year-old spayed female Siamese cat was submitted for necropsy following unsuccessful treatment for obstructive jaundice. Histopathologic examination revealed an adenocarcinoma of the hepatopancreatic ampulla. The carcinoma obstructed the pancreatic and common bile ducts entering the ampulla, resulting in severe diffuse acinar degeneration, atrophy and fibrosis of the pancreas, and dilatation of the bile ducts, biliary fibrosis, and ductule proliferation in the liver. In humans, carcinoma of the ampulla of Vater, the hepatopancreatic ampulla, is considered an uncommon malignancy.

Key words: Adenocarcinoma; ampulla of Vater; cats; hepatopancreatic ampulla.

A hepatopancreatic ampullary carcinoma was diagnosed in a cat. This is believed to be the first report of a hepatopancreatic ampullary carcinoma in a nonhuman species.

The ampulla of Vater was first described by the German anatomist Abraham Vater in 1720. It is a flask-shaped dilatation formed by the junction of the intramural portion of the common bile duct and the main pancreatic duct of Wirsung proximal to their opening into the lumen of the duodenum at the apex of the major duodenal papilla.^{6,11} In the cat, the common bile duct runs a short distance within the intestinal wall before entering the ampulla. The cat's major duodenal papilla is located on the dorsal internal wall of the

duodenum about 3 cm from the pylorus. About 2 cm caudoventrad to the major papilla is the smaller, minor duodenal papilla, which receives the accessory pancreatic duct.⁵

Bile duct carcinomas have been reported in the dog, cat, pig, horse, sheep, cow, parrot (*Amazona* spp.), sloth bear (*Melursus ursinus*), and pallid bat (*Antrozous pallidus*).^{2,3,7–10,13,14} The majority of these biliary carcinomas were intrahepatic tumors; however, extrahepatic tumors have been reported in the sloth bear, Asiatic bear (*Sclenarctos thibetanus*), and domestic cat.^{1,8,12} These extrahepatic tumors have generally involved the gallbladder, cystic duct, and/or common bile duct.