Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: **183** Month: **February** Year: **2022**

Answer Sheet

Title: Feline panleukopenia in a cat.

Contributors: Igor R. Santos[1], DVM, MS candidate; Franciéli A. Molossi[1], DVM, MS, PhD candidate; Tainah P. Dal Pont[1], DVM, Pathology resident; Marcele B. Bandinelli[1], DVM, MS, PhD; Cláudio W. Canal[2], DVM, MS, PhD; and Saulo P. Pavarini[1], DVM, MS, PhD.

[1]Setor de Patologia Veterinária, Faculdade de Medicina Veterinária, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil. Corresponding author: igor.ozn@gmail.com

[2]Laboratório de Virologia Veterinária, Faculdade de Medicina Veterinária, UFRGS, Porto Alegre, RS, Brazil.

Clinical History: A 7-month-old female domestic shorthair cat was referred to a private veterinary hospital for a history of anorexia and prostration of unknown duration. The cat had no history of vaccination. Physical examination revealed diarrhea and pyrexia (rectal temperature of 40.7°C [105.2°F]). Results of complete blood count included evidence of thrombocytopenia (146 x 10^9 platelets/L; reference range [RR], 230 to 680 x 10^9 platelets/L) and leukopenia (1.3 x 10^9 WBCs/L; RR, 7.7 to 18.6 x 10^9 WBCs/L) characterized by lymphopenia (0.1 x 10^9 lymphocytes/L; RR, 1.3 to 7.4 x 10^9 lymphocytes/L) and neutropenia (1 x 10^9 neutrophils/L; RR, 3.1 to 12.5 x 10^9 neutrophils/L). Tests of circulant feline leukemia virus (FeLV) antigen and anti-feline immunodeficiency virus (FIV) antibody were negative. No significant abnormalities were observed in the serum biochemical profile, thoracic radiography, and abdominal ultrasonography. The cat was euthanized due to a poor prognosis and submitted for postmortem examination

Gross Findings: The cat was in poor body condition and markedly pale mucous membranes. The serosa of the small intestine, especially in segmental areas of the jejunum, was reddened (Fig. 1). On the cut surface, the intestinal wall presented thickening and hose-like turgidity. Contents of the small intestine were yellow, scant, and watery. In addition, the mucosal surface was diffusely covered by strands of yellow fibrillar content and the Peyer's patches were depressed (Fig. 2). Other significant gross lesions included only prominent mesenteric lymph nodes.

Gross and Histological Images:

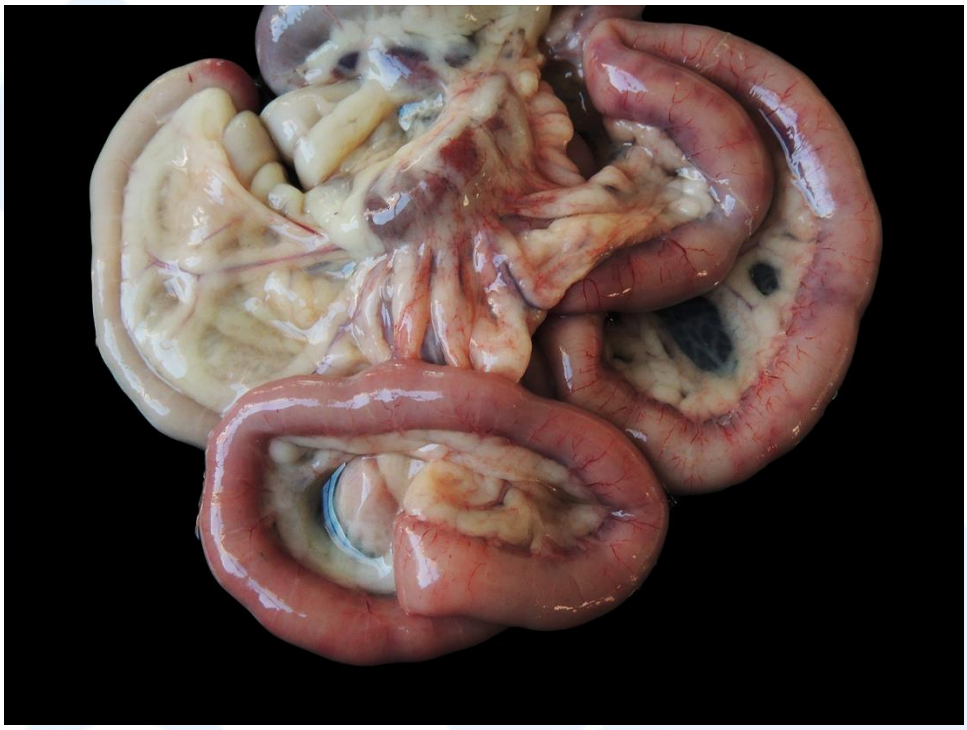

Figure 1. Small intestine and mesenteric lymph nodes, cat. Segmental redness of the jejunum and mesenteric lymphadenomegaly.

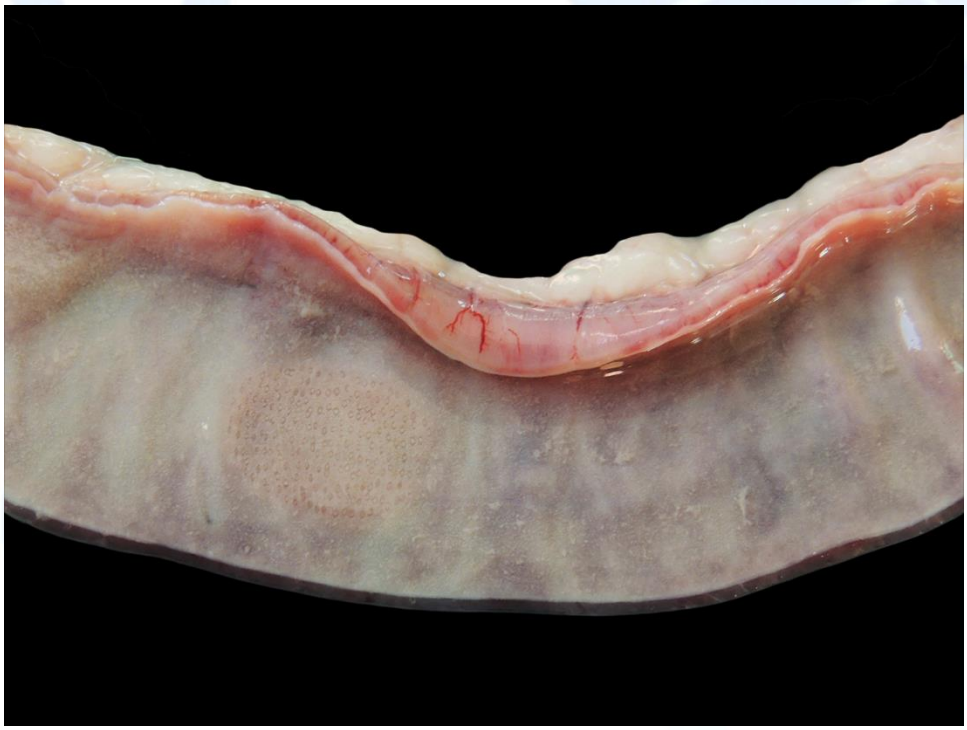

Figure 2. Small intestine, cat. Fine strands of fibrin and depressed Peyer's Patches on the mucosal surface of the jejunum.

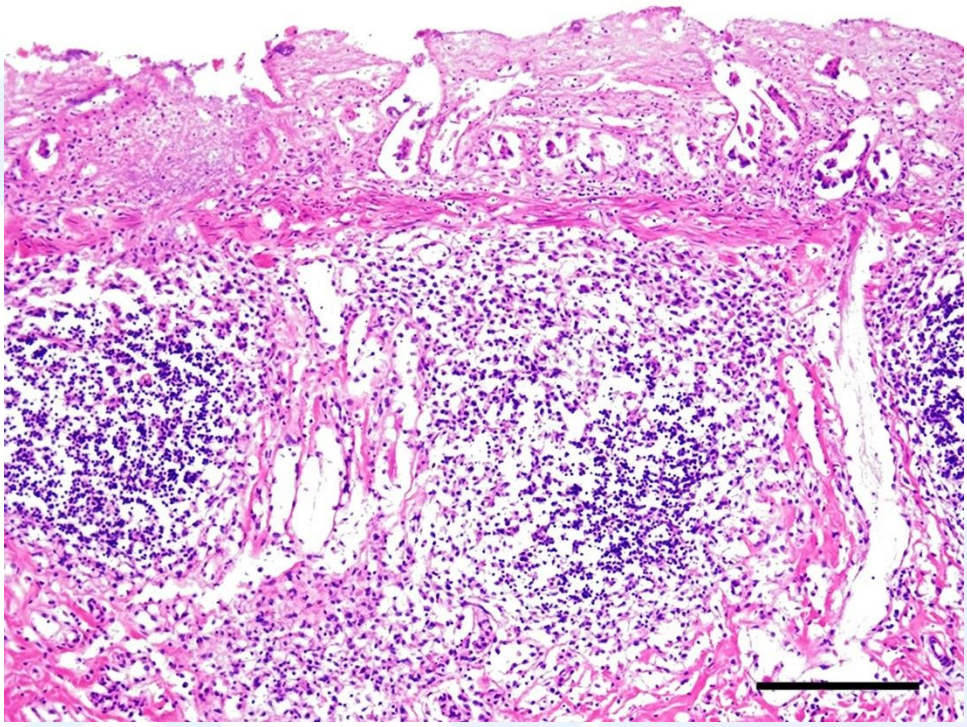

Figure 3. Small intestine, cat. Collapse of the mucosa with severe loss of crypts, mild inflammatory infiltrate, and superficial bacterial colonization. Moderate lymphoid depletion in the Peyer's patches. H&E, bar = 500µm.

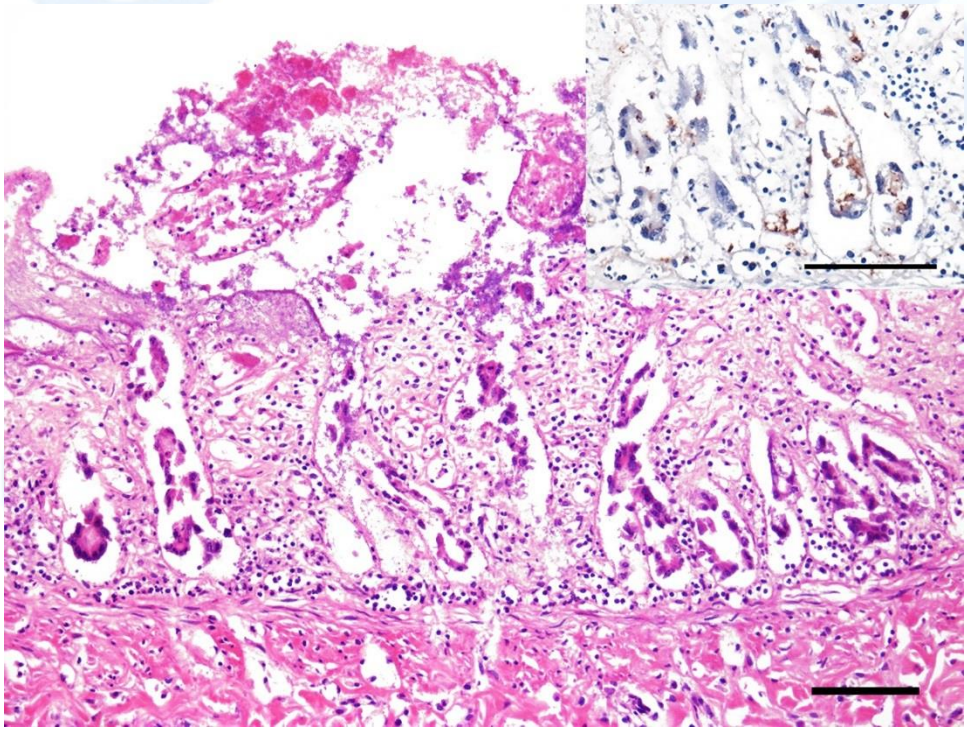

Figure 4. Small intestine, cat. Crypts lined by hypertrophied or attenuated epithelium. H&E, bar = 200µm. Inset: immunoreactivity for parvovirus in the crypt epithelium. Bar = 400µm.

Histological Description: Small intestine: The mucosal architecture was diffusely collapsed due to marked villous atrophy and fusion (Fig. 3). In the affected areas, the crypts were replaced by cellular debris and mild inflammatory infiltrates of neutrophils, lymphocytes, and plasma cells. The remaining crypts were dilated, filled with necrotic epithelial cells, and often lined by hypertrophied or attenuated epithelium (Fig. 4). Marked ulceration associated with fibrin exudation, neutrophilic infiltrate, and numerous colonies of bacilli were observed on the villous surface. Multifocally, the submucosa was distended by mild edema, and the serosa had a mild hemorrhage. Additionally, there was moderate lymphoid depletion and necrosis in the Peyer's patches and multifocal thrombosis.

Morphologic Diagnosis: Enteritis, necrohemorrhagic, diffuse, marked, acute with villous atrophy and fusion, and cryptal necrosis.

Immunohistochemical and Molecular Findings: Sections of the small intestine with representative lesions were submitted to immunohistochemistry (IHC) using an anti-parvovirus antibody. Multifocal, moderate cytoplasmatic immunoreactivity was detected in the affected crypt epithelium (inset of Fig. 4) and occasional lymphoid cells of the Peyer's patches. By real-time PCR assay using primer pairs 555for/555rev, a 583 bp fragment of the VP2 gene (position 4003–4585) of the Carnivore protoparvovirus 1 (CPV-1) was detected on fresh samples of intestinal content.

Possible Etiological Agent(s): Feline parvovirus (FPV) or/and canine parvovirus 2 (CPV-2) variants.

Name of the Condition: Feline panleukopenia.

Comments: The clinical and pathological findings in this case report were typical of feline panleukopenia, also called infectious feline enteritis, feline parvovirus-associated disease, or feline distemper. Feline panleukopenia is a highly contagious clinical disease in cats caused by strains of CPV-1, including FPV (formerly called feline panleukopenia virus) and CPV-2 variants (1). The FPV-induced disease has been reported in cats since the 1920s, and CPV-2 originated from FPV by natural genetic mutation and rapidly spread worldwide as the new dog pathogen in the mid-1970s (7). Over time, new variants of CPV-2 (CPV-2a, -2b, and -2c) emerged and were able to infect and cause clinical disease in cats (6, 9). Co-infection by FPV and CPV-2a in cats has also been described (2). Clinical and pathological findings caused by FPV and CPV-2 variants have many similarities (1, 5). In our case, based only on IHC and real-time PCR results, both FPV and CPV-2 variants were considered possible etiological agent(s). Feline panleukopenia occurs mainly in young animals, frequently in incompletely vaccinated and unvaccinated kittens (1). Lesions reflect the infection in target tissues with a high mitosis activity, such as gastrointestinal epithelium and hematopoietic/lymphoid tissues (5). Oronasal exposure in kittens older than six weeks can result in infection of the tonsils and Peyers' patches, followed by central and other peripheral lymphoid tissues (9). After initial viral replication in lymphoid tissue, the gastrointestinal epithelium is infected through the virus dissemination by cell-free viremia and circulating lymphocytes (3, 9). In the infected crypt enterocytes, the release of the parvoviral particles resulting from the replication cycle kills the cell

(9). Usually, the extent and degree of intestinal damage are determined by the cryptal epithelium's virus availability and proliferation rate.

Moreover, the transplacental infection can result in abortion, mummification, stillbirth, or central nervous lesions in kittens (1). Clinical signs in animals that developed the acute course of feline panleukopenia include diarrhea, vomiting, pyrexia, depression, inappetence, and dehydration with a clinical course of several days (1), similarly to the findings described herein. The hematological findings result from viral lymphocytolysis, lymphocyte migration into tissues, disseminated intravascular coagulation, stem cell depletion, and megakaryocyte destruction (1, 5, 8). All pathological findings in the small intestine observed in our case are classic of feline panleukopenia, although they vary according to the duration and severity of the disease (1). Intranuclear viral inclusions in the intestinal epithelium may be observed in the initial stages of infection (3). Additional histopathological lesions in lymphoid tissue, bone marrow, colon, stomach, liver, lung, and pancreas are occasionally seen (9). Even in cats submitted to appropriate care, the mortality rates of feline panleukopenia are remarkably high (4). Infected cats should be kept in isolation, and the primarily supportive therapy consists of replacement electrolytes, acid-base, and fluid balance (1). Antibiotic therapy for the prevention of septicemia due to secondary bacterial infections is essential and usually attempted with a broad-spectrum antibiotic against anaerobic and gram-negative bacteria (1).

Additionally, antiemetics in cases of persistent vomiting, B vitamin complex supplementation to prevent thiamine deficiency, plasma or blood transfusions to restore oncotic pressure, and gastrointestinal supportive therapies (probiotics and bland diets) during the recovery phase can also be required (8). The efficacy of secondary treatments, such as antiviral drugs, feline interferon-omega, and passive immunotherapy, are not available in cats (1, 4, 8). There are many pathological differential diagnoses for enteritis in cats. Of the infectious causes, feline panleukopenia is the most common disease and must be differentiated from FeLV infections due to the cryptal necrosis in the small and large intestines (9). We ruled out this differential diagnosis based on the negative test of circulant FeLV antigen, on the lymphoid depletion assessed by histopathological examination, tissue positive immunoreactivity for parvoviral antigen, and positive real-time PCR for CPV-1. Although other viral, bacterial, protozoan, and parasitic agents can also cause enteric lesions in cats (e.g., FIV, enteric coronavirus, rotavirus, astrovirus, calicivirus, *Salmonella* spp, *Yersinia enterocolitica*, *Toxoplasma gondii*, *Cystoisospora felis*, *Giardia duodenalis*, *Toxocara cati*, *Ancylostoma* spp, and *Cryptosporidium felis*), they are uncommon and rarely associated with mortality (4, 9).

References:

1. Barrs VR. Feline panleukopenia: a re-emergent disease. Vet Clin Small Anim 2019;49: 651-670.
2. Battilani M, Balboni A, Giunti M, et al. Co-infection with feline and canine parvovirus in a cat. Vet Ital 2013;49: 127-129.
3. Gelberg HB. Alimentary system and the peritoneum, omentum, mesentery, and peritoneal cavity. In: Zachary JF, editor. Pathologic Basis of Veterinary Disease. 6th Ed. St. Louis: Elsevier Saunders;2017. p. 324-411
4. Hall EJ. Small intestine. In: Washabau RJ, Day MJ, editors. Canine and Feline Gastroenterology. St. Louis: Elsevier Saunders; 2013. p. 651-728

5. Lamm CG, Rezabek GB. Parvovirus infection in domestic companion animals. Vet Clin Small Anim 2008;38: 837-850.
6. Miranda C, Parrish CR, Thompson G. Canine parvovirus 2c infection in a cat with severe clinical disease. J Vet Diagn Invest 2014;26: 462-464.
7. Parrish CR. Host range relationships and the evolution of canine parvovirus. Vet Microbiol 1999;69: 29-40.
8. Truyen U, Addie D, Belák S. Feline panleukopenia: ABCD guidelines on prevention and management. J Feline Med Surg 2009;11: 538-546.
9. Uzal FA, Plattner BL, Hostetter JM. Alimentary system. In: Maxie MG, editor. Jubb, Kennedy & Palmer's Pathology of Domestic Animals. 6th Ed. Vol. 2. St. Louis: Elsevier Saunders. 2016. p. 1-257.

*The Diagnostic Exercises are an initiative of the Latin Comparative Pathology Group (LCPG), the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. - Consider submitting an exercise! - A final document containing this material with answers and a brief discussion will be posted on the CL Davis website (https://davisthompsonfoundation.org/diagnostic-exercise/)

Associate Editor for this Diagnostic Exercise: Saulo Pavarini
Editor-in-chief: Claudio Barros.