

❖ PEER-REVIEWED

Feline infectious peritonitis: Typical findings and a new PCR test

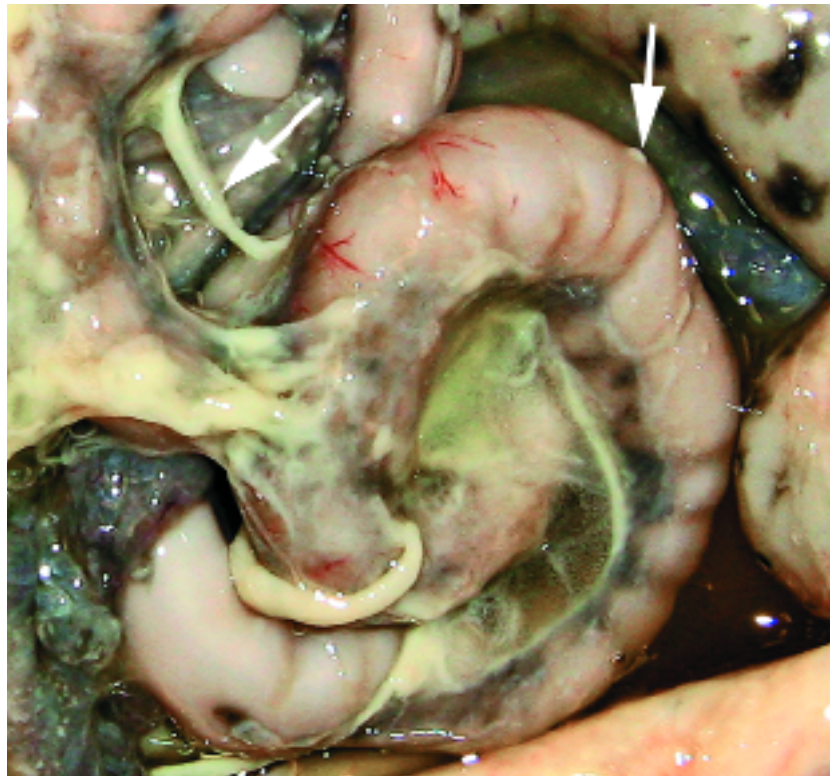
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A 1-year-old castrated male domestic shorthaired cat was presented for evaluation of a 10-day history of lethargy, anorexia, decreased water consumption, and apparent discomfort. A complete blood count and serum chemistry profile revealed hypoalbuminemia, leukocytosis, and neutrophilia. The results of a combined ELISA test for feline leukemia virus and feline immunodeficiency virus were negative.

On presentation, the cat was quiet, alert, and responsive, and it had pale mucous membranes. It also had a distended abdomen and a fluid wave. Abdominocentesis yielded a yellow viscous fluid with a total protein concentration of 4.6 g/dl and a nucleated cell count of 2,500/ μ l with 90% segmented neutrophils. Given the effusion's characteristically high protein concentration and relatively mild inflammatory reaction, we tentatively diagnosed feline infectious peritonitis (FIP) and informed the owners of the poor prognosis. The owners elected euthanasia and gave their consent for a post-mortem examination.

NECROPSY FINDINGS

The peritoneal cavity contained about 500 ml of a viscous, straw-colored fluid with pale-yellow to



1. The peritoneal cavity of a 1-year-old cat suspected of having FIP. Note the pale-yellow and tan strands of fibrin throughout (arrows).

tan strands of fibrin (Figure 1).

There were numerous fibrous and fibrinous adhesions between various organs as well as adhesions between organs and the body wall (Figure 2). The spleen and liver were covered with a thick, yellow-tan fibrinous coating, and numerous smooth, raised, 1- to 2-mm, circular, coalescing, white plaques were noted on the serosal surfaces of the intestines and parietal peritoneum (Figure 2).

HISTOLOGIC FINDINGS

Histologic examination of the abdominal organs demonstrated that the serosal plaques were composed of large amounts of fibrin and inflammatory cells consisting of lymphocytes, plasma cells, and macrophages with occasional clusters of degenerate neutrophils with pyknotic nuclei (Figure 3). The clinical history, gross findings (fibrinous peritonitis), and histologic findings were most consistent with FIP. >

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DISCUSSION

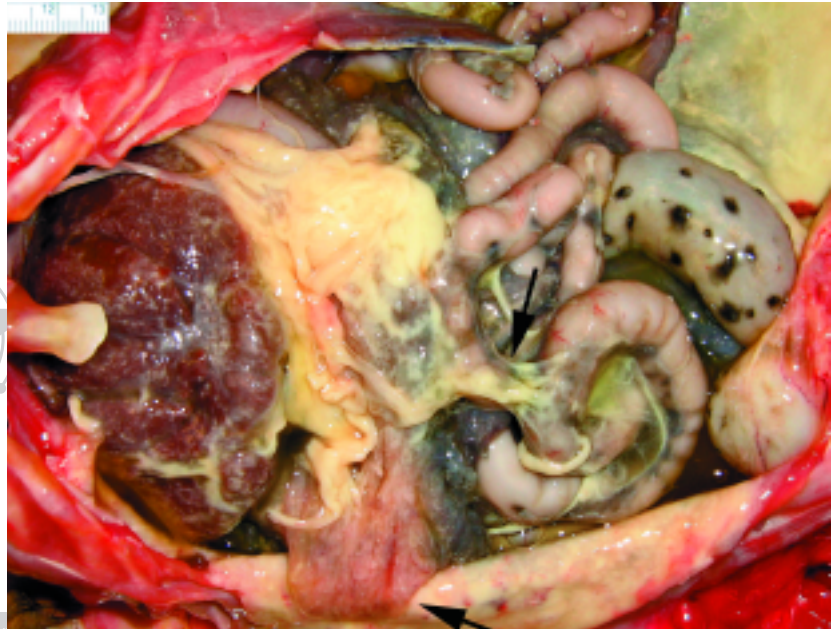
FIP is an immune complex-mediated disease caused by pathogenic feline coronavirus. After pathogenic feline coronavirus infection, the disease progresses quickly. Since systemic antibodies are not protective, development of cell-mediated immunity is the most crucial factor in determining the outcome of this viral infection. Cats that produce humoral antibodies but fail to generate an effective cell-mediated immune response develop effusive FIP. In this effusive form, immune complexes aggregate in the vasculature and attract complement, causing a vasculitis and subsequent transudate.

The classic wet, effusive form, as seen in this case, is characterized by abdominal effusion with strands and mats of fibrin with multifocal serosal pyogranulomas. The dry, noneffusive form is thought to result from a partially protective cell-mediated immune response that is unable to wall off and contain the virus. This dry form is characterized by multiple granulomas or pyogranulomas in various organs including the lungs, liver, kidneys, intestines, and central nervous system. Affected cats often have a combination of both the effusive and noneffusive forms, with one form predominating.

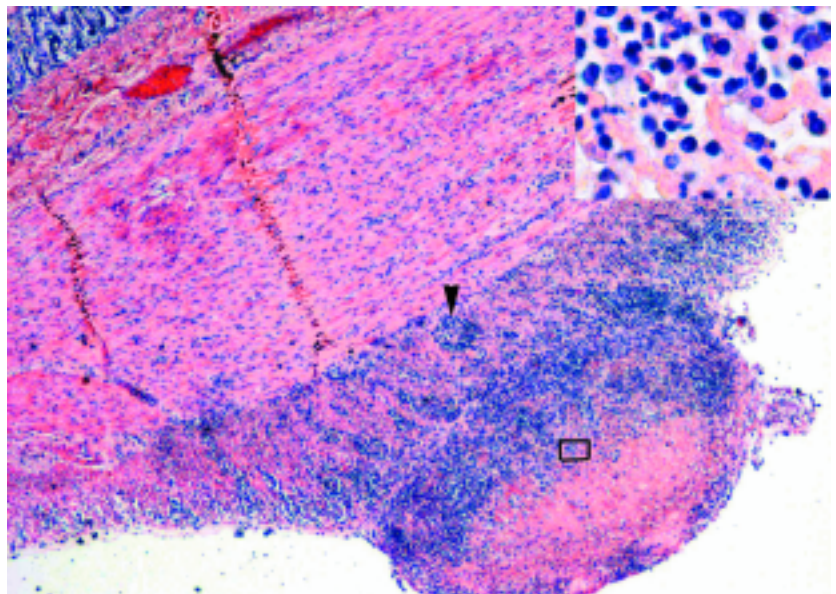
The difficulties of diagnosis

The virus responsible for causing FIP is thought to be a mutant strain of the nonpathogenic feline enteric coronavirus.¹ Since serum antibody tests are unable to distinguish between pathogenic feline coronavirus and the avirulent feline enteric coronavirus, diagnosing FIP is often difficult and frustrating. Traditionally, FIP is diagnosed based on a high antibody titer along with a strong clinical suspicion (*i.e.* lymphopenia, hyperglobulinemia, anemia). The only definitive diagnosis, however, is based on either im-

Cats often have a combination of both the effusive and noneffusive forms.



2. The cat's abdominal cavity showing fibrous and fibrinous adhesions between the organs and the body wall (arrows). Also note the fibrinous covering on the liver's surface. The black serosal plaques on the colon are normal Peyer's patches.



3. A photomicrograph of a serosal plaque from the cat's jejunum showing large amounts of fibrin and inflammatory cells (*inset*). Occasionally, this inflammation could be seen surrounding blood vessels and within the walls of small arterioles (*arrowhead*) (hematoxylin-eosin, 20 \times).

munohistochemical evaluation of surgical biopsy samples or histologic examination of samples obtained postmortem.

The noneffusive form of FIP can be particularly challenging diagnostically because affected animals lack the typical proteinaceous effusion and can present with vague clinical signs. A key feature of the

ther diagnostic testing such as a biopsy or polymerase chain reaction (PCR) testing.

Diagnostic help: A new PCR test

PCR tests for FIP were developed to detect virus particles in whole blood based on the assumption that FIP virus spreads via the bloodstream whereas feline enteric

coronaviruses are incapable of replicating in peripheral blood, no mRNA is produced. FIP virus replicates in monocytes of peripheral blood and, thus, mRNA is produced, which can be detected by using PCR testing. Whole blood is used, and a DNA copy of the M gene mRNA is made using a reverse transcriptase, which then undergoes several amplification steps using primers specific for particular M gene sequences.² The PCR sample is then analyzed with electrophoresis.

FIP virus replicates in circulating monocytes and produces mRNA, which can be detected with PCR testing.

noneffusive form is ocular involvement. Typical changes include iritis (color change), aqueous flare, and retinal changes (occasionally seen as retinal vascular cuffing or pyogranulomas). Although these changes can be seen with feline immunodeficiency virus infection, feline leukemia virus infection, systemic mycosis, and toxoplasmosis, noneffusive FIP should also be considered. Noneffusive FIP often causes pyogranulomas on the surfaces of the kidneys and intestines. If large enough, these nodules can be seen ultrasonographically and during exploratory surgery, but they can be confused with other diseases, most notably lymphoma. Often, the noneffusive form causes variable neurologic signs depending on where the pyogranulomatous inflammation localizes.

Thus, while the noneffusive form of FIP poses a particular challenge diagnostically, the presence of ocular or renal lesions or neurologic signs in addition to risk factors (e.g. cats obtained from catteries, cats that are seropositive for feline coronavirus) should raise the suspicion for FIP and warrant fur-

ther diagnostic testing such as a biopsy or polymerase chain reaction (PCR) testing. coronavirus remains in the intestinal epithelium.² Unfortunately, virus particles can still be detected in the blood of healthy cats with feline enteric coronavirus, suggesting that small numbers of feline enteric coronavirus particles do circulate but are unable to replicate or cause problems outside of the intestinal tract.³

A new PCR test seems to better differentiate FIP from feline enteric coronavirus infection. It takes advantage of the fact that the pathogenic feline coronavirus is able to replicate within mononuclear cells within the blood, whereas feline enteric coronavirus may be able to enter the bloodstream but is not able to replicate outside of the intestinal tract.

Detecting active virus replication.

The PCR test detects messenger RNA (mRNA) of the M gene of feline coronavirus. The M gene is a highly conserved viral gene that is only expressed (*i.e.* mRNA is produced) during viral replication.² Detection of actively replicating virus particles in the blood is thought to be specific for FIP.² Since enteric

Drawbacks of PCR testing. One major drawback of this test is related to the inherent difficulties of PCR testing. The likelihood of inaccurate results increases if the test is not performed properly (risk of contamination) or if adequate controls are not used. The use of appropriate primers are necessary to identify gene segments specific for coronavirus. Other reasons for inaccurate results include the number of virus strains and the rate of mutation of the viral genes.² Fortunately, the M gene is highly conserved among the coronaviruses and false negative results are low. The other major drawback of PCR is the potential consequence (*i.e.* euthanasia) of a false positive result, so the results of any PCR test should be carefully interpreted in the context of clinical suspicion and not relied on solely for diagnosis.

New PCR test availability. The PCR test is available from the College of Veterinary Medicine at Auburn University.* Although the new PCR test holds promise for a more accurate diagnosis of FIP, it has not been widely used clinically to determine its ease of use, cost effectiveness, and reliability.

*Molecular Diagnostics, College of Veterinary Medicine, Auburn University; www.vetmed.auburn.edu/index.pl/feline_infectious_peritonitis_virus.

CONCLUSION

FIP is an unusual and often fatal consequence of feline coronavirus infection in cats. It is an infectious disease for which there is no effective treatment and for which the mortality rate is 100%. Despite ongoing research in this field, it remains a disease of much controversy and confusion. ♦

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