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Pathology in Practice

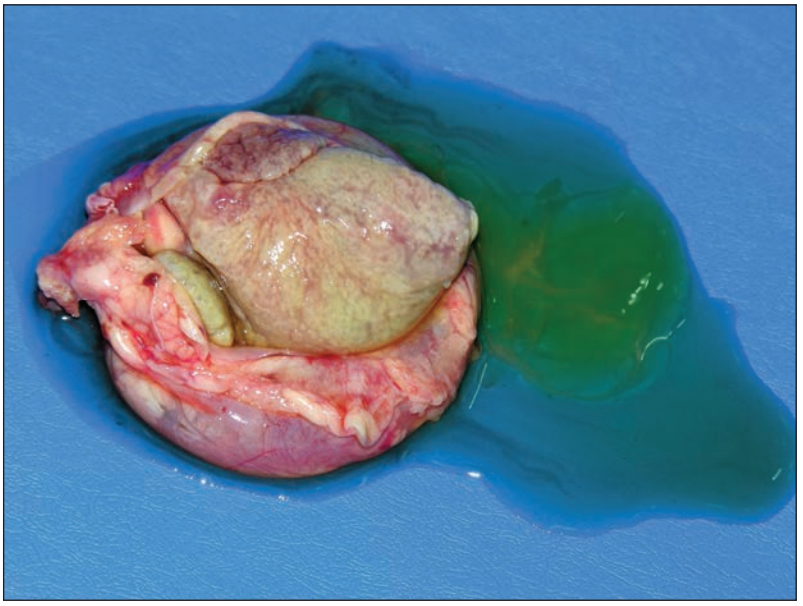

Figure 1—Photograph of the opened pericardial sac and heart of a 1-year-old cat that developed inappetence and lethargy and subsequently was euthanized. The pericardial sac is thickened and filled with yellow gelatinous fluid. The epicardial surface is covered by an adherent layer of fibrin.

History

A 1-year-old 3.68-kg (8.1-lb) calico spayed female domestic shorthair cat was referred to the University of Georgia Small Animal Teaching Hospital with severe inappetence and lethargy. The cat had a history of anemia due to *Mycoplasma* infection and had been treated with doxycycline and prednisone.

Clinical and Gross Findings

At initial evaluation, the cat was severely hypothermic (rectal temperature was below detection limit on the thermometer) and had low blood pressure (50 to 60 mm Hg; reference interval, 110 to 160 mm Hg), severe anemia (14%; reference interval, 30% to 45%), and hypoglycemia (blood glucose concentration was less than the detection limit of the laboratory test). Abdominal and thoracic ultrasonography revealed abdominal and pericardial effusion, respectively, and an aspirate of the abdominal effusion had total solids concentration of 3.8 g/dL. The cat's blood pressure did not respond to repeated IV administrations of colloid and crystalloid fluids. On the basis of generalized cavitary effusion, prognosis was deemed poor and the cat was euthanized by means of an overdose injection of pentobarbital-phenytoin solution.

On gross examination, the cat was markedly dehydrated and in fair body condition (body condition score, 3/9); the cavitary fat deposits were moderately decreased. The thoracic cavity contained moderate amounts of serosanguineous fluid, and fibrin covered the parietal and visceral pleural surfaces. The pericardial sac was expanded and filled with moderate amounts of yellow, viscous to gelatinous fluid. The epicardial surface was diffusely thickened by an adherent layer of fibrin (**Figure 1**). The abdominal cavity was filled with viscous to gelatinous yellow fluid. Multifocally, the surfaces of the diaphragm, intestinal loops, mesentery, spleen, liver, and urinary bladder were covered by fibrin.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

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Histopathologic Findings

Heart, lung, spleen, intestine, and brain specimens were fixed in neutral-buffered 10% formalin and processed routinely for histologic evaluation. The epicardium was diffusely expanded by a mat (approx 700 µm in width) of eosinophilic, fibrillar material (fibrin) admixed with cellular and karyorrhectic debris, viable and degenerated neutrophils, macrophages, numerous plasma cells, and fewer lymphocytes (**Figure 2**).

The visceral pleura was expanded and lined by mats of fibrin, cellular and karyorrhectic debris, numerous neutrophils, plasma cells, and macrophages. Similar mats covered the hepatic and splenic capsules and the mesenteric surfaces of the intestine. Diffusely, the alveolar spaces of the lungs were filled with edematous fluid.

Infiltrating the wall and extending into the perivascular spaces of scattered medium-sized mesenteric arteries were moderate numbers of lymphocytes, plasma cells, fewer macrophages, and neutrophils along with fibrin and necrotic cellular debris; a few arteries were thrombotic. In the liver, acute centrilobular coagulative necrosis, diffuse moderate hepatocellular lipidosis, and scattered plasma cells and lymphocytes within the portal areas were evident.

Immunohistochemical staining for feline infectious peritonitis (FIP) virus (FIPV) was performed on samples of heart, lungs, spleen, intestines, and mesentery with a commercially available antibody[a] as previously described.[1] For each sample, a portion of the same tissue was processed with mouse isotype control serum instead of the primary antibody (negative control); also, lymph node tissue from a cat with FIP (confirmed by results of fluorescent antibody testing) underwent immunohistochemical staining (positive control). Results of the staining indicated that the cytoplasm of numerous macrophages within the epicardial exudate as well as the cytoplasm of macrophages within the exudate on the serosal surfaces of the lungs, spleen, intestines, and mesentery was FIPV positive.

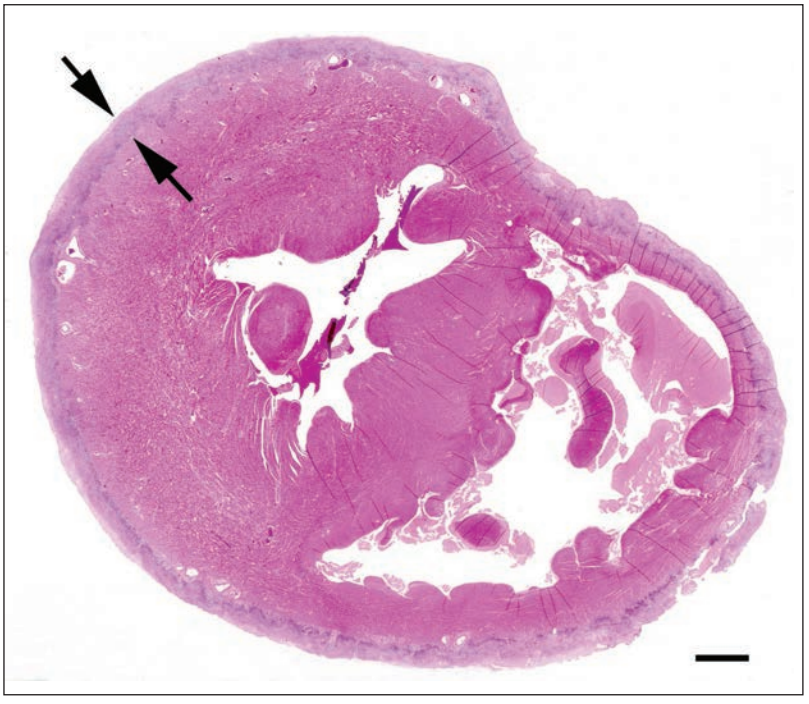

Figure 2—Photomicrograph of a cross section of the entire heart of the cat in Figure 1. The epicardium is circumferentially expanded by a thick layer of fibrin admixed with inflammatory infiltrate and cellular debris (between arrows). H&E stain; bar = 0.16 cm.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: severe, fibrinous, lymphoplasmacytic and pyogranulomatous epicarditis and polyserositis and severe, multifocal, necrotizing lymphoplasmacytic mesenteric vasculitis with thrombosis (consistent with FIP); and moderate acute centrilobular coagulative hepatic necrosis and hepatic lipidosis.

Case summary: effusive FIP with fibrinous epicarditis in a cat.

Comments

On the basis of multicavitary effusions and fibrinous polyserositis, a diagnosis of the effusive form of FIP was made for the cat of this report. Numerous macrophages that were FIPV positive, as detected via immunohistochemical staining, confirmed the diagnosis. The severe anemia, along with pericardial and thoracic effusions, contributed to hypoxia, which led to the centrilobular hepatic degeneration and necrosis.

Feline infectious peritonitis is a disease of cats caused by FIPV, which is a type of feline coronavirus (FCoV); along with feline enteric coronavirus (FECV), FCoV is classified in the genus *Coronavirus*, family *Coronaviridae*, order Nidovirales. Feline coronaviruses are enveloped, single-strand, positive-sense RNA viruses.[2]

Feline infectious peritonitis virus initially replicates in the intestines or tonsils and subsequently in the regional lymph nodes. The virus proliferates within the macrophages and is carried by these cells to various sites in the body, leading to systemic infection.[3] In a given animal, the outcome of FIPV infection strongly correlates with the effectiveness of cell-mediated immunity and the concentrations of interferon-γ produced on infection. It has been hypothesized that cats with weak cell-mediated immunity associated with a strong humoral immune response develop clinical FIP, whereas cats with strong cell-mediated immunity may not develop the disease. Most likely, the antibodies produced against the virus are not protective, owing to the lack of viral antigen expression on the surface of monocytes and macrophages that are preferentially infected by the virus.[4] In addition, it is known that cats with clinical FIP have low serum interferon-γ concentrations, compared with concentrations in cats that do not develop the disease.[5] In infected animals, FIPV infection can be cleared when strong cell-mediated immunity is associated with high serum concentrations of interferon-γ.[5,6]

Morphologically, FIP can develop into wet (effusive) or dry (noneffusive) forms, which become established when the immune response is predominantly humoral or the cellular immunity is too weak (partial immunity), respectively.[5] The effusive form of FIP is considered the most common. Although the 2 forms are distinct, they can be considered as the 2 extremes of a continuum.[5] The development of lesions during the course of FIP is driven by type III hypersensitivity reaction (Arthus reaction) against the viral antigen, which leads to formation of antigen-antibody complexes within the

vascular wall of small vessels, subsequent activation of complement, vascular leakage (edema), necrosis, and perivascular influx of virus-laden macrophages, neutrophils, lymphocytes, and plasma cells.[3,5,7] This immune-mediated vasculitis results in leakage of protein-rich fluid from the blood vessels into the body cavities (wet form) or can result in development of multiple perivascular pyogranulomas in various organs without effusions (dry form).[5] The noneffusive form may become effusive in the terminal stages of the disease.[5]

Although FCoV is easily inactivated by most household detergents and disinfectants, it can survive for 7 weeks in a dry environment and transmission may occur directly or indirectly (via fomites) to other cats.[8] Feces are the main source of FCoV, and the principal source of infection via the oral route in groups of cats is litter boxes.[6,8] Because the virus is rarely found in saliva of healthy cats, there is a minimal risk of transmission in groups with close contact such as sharing feeding bowls.[8] Although rare, transplacental transmission of FIPV to fetuses from a queen with FIP during pregnancy has been described.[8] The prevalence of FIP is high among young cats[1,6] originating from catteries and shelters (ie, crowded environments).[5] Most deaths as a result of FIP occur in cats approximately 1 year of age and are uncommon in cats > 5 years of age.[5]

The most characteristic clinical sign in the effusive (wet) form is a distended abdomen.[6] Dyspnea, tachypnea, and muffled heart sounds develop as a result of thoracic and pericardial effusions.[8] Serositis can involve the tunica vaginalis of the testes, leading to scrotal enlargement.[5,6] The most prominent gross postmortem finding in cats with the effusive form is fibrinous polyserositis, characterized by large amounts of yellow-tinged, slightly to moderately cloudy, mucinous (protein-rich) fluid in the abdominal and thoracic cavities associated with small (1- to 2-cm) white plaques on the serosal surfaces of multiple organs.[5] Fibrinous epicarditis, as seen in the cat of this report, is uncommon.[8]

The noneffusive (dry) form in cats is characterized by perivascular pyogranulomas in multiple organs and is often more difficult to diagnose, with specific clinical signs depending on the organs involved. Fever, anorexia, and lethargy may be the only signs, particularly in the early stages of disease.[8] The dry form usually affects the kidneys, eyes, and CNS (mainly the brain).[1,6,8] On abdominal palpation, the kidneys may be enlarged (renomegaly). At postmortem examination, the surface of the kidneys may have a nodular surface, and multiple small to large pyogranulomas are frequently found in the kidneys and mesenteric lymph nodes.[5] Ocular involvement results in uveitis, leading to changes in iris color, keratic precipitation, dyscoria or anisocoria secondary to iritis, sudden loss of vision, and hyphema.[5,6,8] The most common neurologic signs are ataxia, hyperesthesia, nystagmus, seizures, behavioral changes, and cranial nerve deficits due to meningitis, choroid plexitis, and acquired hydrocephalus.[1] An uncommon form of dry FIP is associated with a pyogranulomatous mural mass in the colon or at the ileocecocolic junction, which mimics alimentary lymphosarcoma.[9] Cutaneous signs in an FIPV-infected cat have recently been reported, characterized by multiple nodular lesions caused by pyogranulomatous and necrotizing dermal phlebitis and skin fragility.[10] In cats, a diagnosis of FIPV infection is made on the basis of a combination of history, clinical signs, results of clinicopathologic testing and other supportive diagnostic tests (including serologic evaluation), imaging, examination of tissue biopsy specimens, and PCR assay for FIPV.[8]

Microscopically, the hallmark lesion of FIP (both for wet and dry forms) is a vasocentric pyogranulomatous inflammation.[3,7] Pyogranulomatous inflammation is characterized by large focal or numerous small inflammatory infiltrates containing mainly macrophages and neutrophils with scattered lymphocytes and plasma cells, which are mostly centered around vessels with transmural fibrinoid necrosis.[3,7] In cats with either form of FIP, immunohistochemical analysis has been used to detect FCoV antigen within the cytoplasm of macrophages; when the result is positive, it is 100% diagnostic for FIP.[7,8]

Feline infectious peritonitis is fatal in most cases, and cats with clinical FIP inevitably die in days, weeks, or months.[8] Treatment is not very effective, but there are occasional reports of cats surviving for several months after diagnosis.[6] The differential diagnoses for the effusive form of FIP are bacterial or mycotic peritonitis and pyothorax, and the noneffusive form must be differentiated from lymphosarcoma, steatitis, mycotic infections, and toxoplasmosis. It is important to prepare the owners for the unfortunate outcome that inevitably follows the diagnosis of FIP in a cat. Supportive care with immunosuppressive and anti-inflammatory drugs is recommended as long as the cat's quality of life is not compromised.[8]

a. Anti–FIPV3-70 antibody, Custom Monoclonals International, West Sacramento, Calif.

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