

Feline Infectious Peritonitis: A Confusing Diagnosis

Alexandra Myers, Texas A&M University, Class of 2015

Abstract

Feline infectious peritonitis (FIP) is a dreaded and deadly viral illness of young cats. The disease is complex and still poorly understood which has made diagnostics and treatment a veterinarian's nightmare since the discovery of the disease in the mid-1900s. Researchers are still actively searching for the exact mutation or mutations that allow the relatively benign feline enteric coronavirus (FECV) to become so virulent so quickly.² Once the mutation is found, it should be much easier to test for the virulent strain and to develop an effective vaccine. Until then, veterinarians are stuck with several confusing diagnostic tests, none of which are totally accurate or reliable. Currently, when a veterinarian can collect an effusion or lymph node aspirate, the fluorescent antibody test for FIP is one of the best, least invasive ways to obtain a convincing diagnosis. When a biopsy can be obtained or post-mortem examination performed, immunohistochemistry is considered to be the most definitive test. Having a firm diagnosis allows the veterinarian to feel more comfortable when giving owners the bad news about this difficult disease.

Introduction

Feline infectious peritonitis (FIP) has always been a challenging disease both diagnostically and therapeutically. Despite a flurry of ongoing research, there is still no effective diagnostic protocol or cure. This article provides an update on what we know about the pathogenesis of this disease and the recommended diagnostic tests.

Pathogenesis

FIP is caused by a mutant form of the ubiquitous and relatively benign feline enteric coronavirus (FECV). While FECV can replicate within blood monocytes/macrophages to a degree, certain mutations allow the virus to begin replication within a specific subset of monocytes/macrophages that have an affinity for the endothelium of venules in the serosa, omentum, pleura, meninges and uveal tract.⁶ Morbidity occurs after this switch in viral tropism, and the virus becomes known as FIP virus. Many mutations between FIP virus and FECV have been found, but the exact mutation(s) that cause the switch to virulence have yet to be identified.

FIP is said to have both a "wet" form and a "dry" form, and the reason for the difference in appearance is thought to stem from the host immune response of the infected cat. Cats that resist the disease entirely are thought to mount a mostly cell-mediated response. The wet form often occurs after a mostly humoral type immune response with high antibody production; this creates a type III hypersensitivity reaction with vasculitis. Antibodies also make it easier for macrophages to consume FIP virus, allowing the virus to replicate and travel through the body. The dry form is thought to occur when the cat mounts a mixed immune response, but has enough T-cell response to confine the virus to macrophages in a few focal areas. Unfortunately, the dry form is often much more difficult to diagnose, but the best diagnostic options will be presented below.

Clinical Signs and Lesions

When the classic clinical signs are seen in a cat of a particular signalment, it can be relatively easy to diagnose FIP. Although any age or breed of cat can acquire the disease, the most common signalment is a young cat (6 months to 2 years) of a certain breed such as British Shorthair, Devon Rex, Birman, Burmese, or Abyssinian.^{1,7} The first lesion to appear is a granulomatous phlebitis caused by the interaction between infected monocytes and endothelial cells. The monocytes are induced to produce cytokines and enzymes that begin to dissolve the vascular basement membrane, leading to an outpouring of fluid from the vessel.⁶ At this point, the veterinarian can often identify ascites or pleural effusion in the patient. If exploratory surgery or necropsy is attempted, the findings would include severe peritonitis with deposition of granular gray-white exudate on the serosal surfaces of abdominal organs.⁷ In cases of dry FIP, other signs such as intraocular and neurologic disease may be all the veterinarian sees.⁵ FIP should be a differential for uveitis or neurologic signs in a young cat.

Certain blood abnormalities are common with FIP such as lymphopenia, anemia, increased total protein due to hypergammaglobulinemia, and increased kidney and liver values.¹ One other classic feature of FIP is an undulating fever that is unresponsive to antibiotics.⁵

Diagnostics

The numerous diagnostic options available to clinicians can be daunting. The disease can be diagnosed with some certainty based on signalment and clinical signs alone; however, given the severe nature of the disease, owners and veterinarians often want to be absolutely sure of the diagnosis. There are two categories of tests when it comes to diagnosing FIP: Direct and indirect. Direct tests are designed to identify the virus in diseased tissue, whereas indirect tests can only tell that it is more or less likely that FIP is the cause of disease.⁵ Examples of indirect tests would be albumin:globulin ratio, coronavirus antibody titers, ultrasonography, effusion analysis, the Rivalta test, and the alpha-1 acid glycoprotein (AGP) test. Direct tests include PCR on diseased tissues/effusions and immunostaining methods.⁵ When clinical signs, signalment, and indirect tests are not enough, and a clinician wants to have the best chance of getting a definitive answer, a direct test would be the best choice:

Direct Tests and Samples Required

- Fluorescent antibody (FA) – effusion, biopsy, lymph node aspirates (**Fresh or frozen**)
- Immunohistochemistry – biopsy or post-mortem (**Formalin-fixed**)
- PCR – effusion or biopsy (**Fresh or frozen**)

The benefit of the FA test is that it allows the virus to be seen fluorescing within macrophages in diseased tissue or effusion. A recent study performed at Purdue's ADDL in 2013 showed that the test is excellent at identifying FIP in effusion fluid.³ If an effusion is present, or aspirates can be obtained, this fluorescent antibody test is currently the best, least invasive choice for providing a diagnosis. PCR may be useful, but no protocol has been developed that can reliably distinguish between FECV and FIP virus.⁵ FECV, though it is mostly an enteric virus, has been found in several other internal organs, and can easily confuse the diagnosis.⁵ A positive PCR test would be most convincing if it were run on a granuloma or effusion from a cat with compatible clinical signs and signalment.

Conclusion

FIP is often suspected based on clinical signs, signalment, and indirect tests, but when a veterinarian needs a definitive answer, it can be difficult to know which test to choose. When an effusion or aspirate

can be obtained, the FA test for FIP is a great option offered by the Purdue ADDL. Seeing the coronavirus fluoresce within effusion is a convincing sign that it is causing disease. PCR is another option offered by some labs that can provide an accurate diagnosis if performed on the right samples. Having a firm diagnosis allows the clinician to proceed with confidence and to feel more comfortable when advising owners about their options.

References

1. Kipar, A. and Meli, M.L. Feline infectious peritonitis: still an enigma? *Veterinary Pathology*. 2014; 51(2): 505-526.
2. Licitra, B. N., et al. Mutation in spike protein cleavage site and pathogenesis of feline coronavirus. *Emerging Infectious Diseases*. 2013; 19(7): 1066-1073.
3. Litster, A. L., et al. Diagnostic utility of a direct immunofluorescence test to detect feline coronavirus antigen in macrophages in effusive feline infectious peritonitis. *Vet J*. 2013; 198(2): 362-366.
4. Rohrbach B.W., et al. Epidemiology of feline infectious peritonitis among cats examined at veterinary medical teaching hospitals. *J Am Vet Med Assoc*. 2001; 218(7):1111–1115.
5. Pedersen, N. C. An update on feline infectious peritonitis: Diagnostics and therapeutics. *Vet J*. 2014;
6. Pedersen, N. C. An update on feline infectious peritonitis: Virology and immunopathogenesis. *Vet J*. 2014;
7. Pesavento, P. A. and Murphy, B. G. Common and Emerging Infectious Diseases in the Animal Shelter. *Veterinary Pathology*. 2014; 51(2): 478-491.