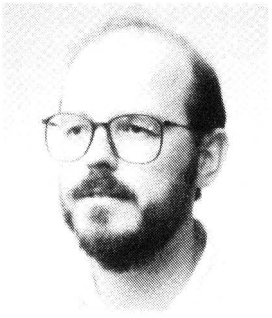
FIP, EASY TO DIAGNOSE?



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INTRODUCTION

Feline infectious peritonitis virus (FIPv), a member of the family Coronaviridae, causes a severe, often fatal disease in domestic and wild felidae. Despite considerable research several questions related to pathogenesis, prevention, and control remain unsolved. Also, no routine method for making a diagnosis in a diseased animal is available. The main reason for this is that feline coronaviruses (FCoV) differ widely with respect to virulence. Some isolates cause FIP in almost 100% of experimentally infected animals, whereas others cause only mild enteritis or subclinical infections (6,7). Because these feline coronavirus strains are serologically and genetically closely related, no routine assay is available to make a distinction (3,5).

Feline coronaviruses are widespread among cats, as indicated by the high prevalence of antibodies against the virus. In catteries and multicat households 80-90% of the cats have antibodies and in single cat households 10-50% of the cats do (1,2,9). FIP occurs in 5-10% of the animals living in catteries and probably in less than 1% of the general population. Therefore it has been suggested that most cats become infected with low virulence strains. FIP could develop in cats in which minor mutations in avirulent strains could generate a more virulent phenotype. Alternatively, virulent strains could be common but only induce FIP if factors such as the virus dose, age, genetic susceptibility of the host, and quality and quantity of the immune response are favorable.

DIAGNOSIS

In practice it is difficult to establish the diagnosis of FIP. Usually, several clinical, hematological and chemical parameters are monitored to establish a presumptive diagnosis. Symptoms indicative of FIP are anorexia, chronic unresponsive fever, lethargy, weight loss and peritoneal and pleural effusion. If effusion is present and consists of a typical exudate the diagnosis is usually made. Laboratory abnormalities frequently found in cats with FIP include a mild to moderate normochromic, normocytic, non-regenerative anaemia, neutrophilic leucocytosis with left shift, and lymphopenia. Serum chemistry often reveals hyperbilirubinemia, elevated ALT levels, hyperglobulinemia, hypoalbuminemia, and decreased albumin/globulin ratios. Increased urea and creatinine levels indicate kidney involvement. Although helpful in the establishment of a diagnosis of FIP none of these laboratory abnormalities are specific for the disease (9,10).

Although serology is still used as a diagnostic tool its value is very limited. A positive coronavirus titre is only indicative for a previous infection with a coronavirus. High titers (>640) are found frequently in cats with FIP but also in asymptomatic cats. Therefore, serology can never be used to establish a definite diagnosis of FIP. At present a definite diagnosis of FIP can only be established by histopathologic examination of biopsy or post mortem material. There is a need for a routine assay for diagnosis of FIP. A polymerase chain reaction to detect feline coronavirus RNA directly in the blood of cats has been developed. The assay has the advantage of detecting an ongoing infection (4). If, as has been hypothesized, only FIP-inducing strains cause systemic infections, the detection of viral RNA in plasma or serum by PCR could discriminate between cats with FIP and those with subclinical feline coronavirus infections. The PCR is an in vitro method to amplify specific DNA sequences, using two oligonucleotide primers that hybridize to the opposite strands. To detect viral RNA, a first necessary step of reverse transcription into DNA is needed. The diagnostic potential of this assay was studied.

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DESIGN OF THE STUDY

Clinical specimens

Blood samples of cats with a presumptive diagnosis of FIP were collected in practice. Ascitic or thoracic fluid was also tested if available. The clinical course was followed and in case of euthanasia, post mortem examination was performed if possible. The results of histopathology were used to confirm or exclude the clinical diagnosis of FIP. Pathology data were obtained from 70 cats. Also blood of 113 healthy cats from catteries with a history of FIP was screened for the presence of FCoV RNA.

PCR methodology

The PCR was performed as described previously (4). Viral RNA was extracted from the plasma using a simple guanidinium thiocyanate-silica concentration step. After reverse transcription the samples were subjected to two rounds of amplification (nested PCR). The primers used are specific for the 3'non-translated region of the viral genome, yielding short amplification products of 223 and 177 bp for the first and the second PCR, respectively. The samples were analyzed in 2% agarose gel. Samples revealing a band of 177 base pairs were considered positive for FCoV RNA. Confirmation was performed by DraI restriction enzyme digestion which yielded specific products of 35 and 142 bp.

RESULTS AND DISCUSSION

The results are summarized in Table 1.

Postmortem histological data were obtained from a total of 70 cats. In 42 of the cats lesions were found indicative of FIP; in 28 cats another disease was confirmed. Of the 42 cats 30 (70%) were positive for coronaviral RNA in the plasma. In an additional 5 cats, plasma was negative but ascitic fluid was positive. In total 35 of 42 cats (83%) yielded a positive

Table 1. Results of PCR in plasma and/or ascitic fluid in 183 cats.

	FIP	non FIP	Healthy
PCR +	35 (83%)	3 (11%)	2 (2%)
PCR -	7 (17%)	25 (89%)	111 (98%)
Total	42	28	113

result. Only 3 of the 28 non-FIP cases and two of 113 healthy cats were corona-PCR positive. One of the healthy cats was a queen that had a litter of which all the kittens died of FIP.
As expected, coronaviral RNA was detected in the majority of cats with FIP. A positive result of the PCR in a sick animal seems to be a better indicator for FIP than serology. In our study only 30% of the cats with FIP had titers of 640, whereas the same titers were found in 20% of the healthy cats (data not shown). A positive PCR result in a plasma sample from a sick animal makes FIP more likely; a negative result does not exclude FIP. However, since some positive results were obtained from cats with other diseases and in healthy cats, the reliability of a positive PCR result does not provide a definite diagnosis of FIP. Further studies are needed to locate the tissues where the virus is harbored in the non-FIP cats: minor lesions could be present. Alternatively, these cats could be virus negative, since they were seronegative as well. The PCR result should then be interpreted as a false positive reaction. Also the value of the PCR for the identification of asymptomatic carriers in the management of catteries should be studied.

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CYTOSTATIC TREATMENT IN VETERINARY MEDICINE

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CLINICAL USE OF CHEMOTHERAPEUTIC AGENTS

In considering the application of chemotherapy to animals with cancer the following factors are of importance: 1. treatment set-up, 2. type of patient, 3. type of tumor, and 4. the owner's view

Treatment set-up

By treatment set-up we refer to whether cytostatic drugs are given solely or in combination with other treatment modalities. The latter is called adjuvant chemotherapy (CT) and its potential value depends upon the efficacy of the combined forms of treatment. In veterinary medicine adjuvant CT is most often used in combination with surgery of tumors that are expected to have developed micrometastases at the time of treatment of the primary lesion, e.g., osteosarcoma in the dog. In general, the period of treatment is limited. The set-up of treatment also includes its aim and potential. CT may aim at killing of all tumor cells, i.e., curative CT, or at a reduction of the tumor mass and the related symptoms, i.e., palliative CT. Curative CT is seldom attempted in veterinary oncology in view of the high treatment intensity often needed and the related toxicity. However, in some lymphomas in the dog and cat and in almost all of condylomas in the dog, a cure may be achieved.
On the other hand, CT can often achieve a palliation of symptoms of a cancer for up to several years. These symptoms include physical distress due to the tumor mass or its infiltrative or metastatic growth, or due to paraneoplastic effects (eg, hypercalcemia due to lymphoma, hypoglycemia due to insulinoma). However, even if effective, it may take some time before CT leads to a reduction in tumor-related morbidity.

Type of patient

Various patient characteristics and interrelations with the therapy must be considered. These include the use of the dog, e.g., breeding, guarding or racing, and the life expectancy with and without the tumor disease. Life expectancy relates to age (although not a contra-indication in itself), clinical performance, function of critical organs, and clinical stage. The presence of another unrelated disease may have influence. The clinical performance for pet animals tries to describe the ability of the animal to exert its normal activities

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