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Feline Leukemia Virus and Feline Lymphosarcoma

by Glenna Rasmussen, DVM*

SUMMARY

Lymphosarcoma, caused by the feline leukemia virus, is the most common neoplasm of the feline species. The condition occurs in cats of all ages and usually runs a very brief but fatal course. Transmission is both horizontal and vertical with the virus being shed in saliva, urine, feces, and milk. Most frequently observed symptoms include weight loss, depression, anorexia, and fever. The possibility of lymphosarcoma should be considered in any animal having an illness of several weeks duration, which is characterized by the above symptoms and having an associated respiratory condition with signs of sneezing, coughing, and dyspnea.

Fluorescent antibody, ELISA, and FOCMA antibody test are available to detect the virus of virus-induced antibody in blood of affected cats. No feline leukemia virus vaccines are currently available; and though chemotherapeutic treatment is being explored, lymphosarcoma should still be considered an incurable disease at the present time.

INTRODUCTION

The feline leukemia virus (FeLV) is a single stranded RNA virus classified as an oncorna virus. Its infection in cats is widespread and related to the density of the cat population and to host and environmental factors that influence the severity. Epizootiologic studies indicate that 25-60% of free roaming cats in urban populations are infected with the virus, with only 2-6% remaining chronically infected. In rural cat populations and closely confined single cat households, the infection chronically infected.¹

Feline leukemia virus is contagious from one cat to another and though it appears to be most easily spread to young cats, all are susceptible. The virus is shed in saliva, urine, and feces of infected cats and can occur when a susceptible cat contacts these secretions. Transmission can be through oral and parenteral exposure and can occur when animals groom or bite each other or share litter and food containers. Although queens infected with feline leukemia virus usually have reproductive problems, it has been shown to be passed in utero to their offspring. Blood sucking insects may theoretically also spread the virus. Aerosol transmission is not an important route of exposure in nature, and because the virus does not live long outside the body, the environment is not an important reservoir source.¹²³¹⁰

Following continuous exposure, virus or antibody to virus is not detectable until four weeks. By twenty weeks, 80% of the cats have been infected. A small percentage, especially if they are older, may not show evidence of infection until 52 weeks.

The pathogenesis of FeLV infection can be divided into three stages: primary disease (apparent or inapparent); death, recovery, or apparent recovery; and recurrent or terminal illness. Often the primary disease is totally inapparent, in which case the virus is eliminated and the cat becomes free of infection. These cats may never be detectably viremic or may be viremic for several weeks. Cats that are ill at this time may show fever, malaise, anorexia, lymphadenopathy, leukemia, and thrombocytopenia. Clinical signs persist for 2-16 weeks, with some cats dying. Most cats that are ill during the primary stage appear to recover but will remain chronically infected.

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These cats that are chronically viremic may eventually (within weeks, months, or years) develop a wide variety of seemingly unrelated diseases or suffer from recurrence of the primary myelosuppression. With symptomatic care and prevention of undue stress, the mortality rate in chronically viremic cats may be kept to 20% per year.

Studies have shown that the more severe the primary illness, the more likely it is that the cat will become chronically viremic. In nature, most infected cats develop inapparent or mild primary illness and recover. In cateries and multiple cat households, the primary illness is likely to be severe and the proportion of cats developing a chronic infection higher.

The FeLV causes lymphosarcoma, lymphocytic leukemia, myeloproliferative diseases, and is also implicated directly in other infectious diseases. Feline lymphosarcoma is the principal tumor caused by FeLV and consists of solid masses of proliferating lymphocytes. One study reports the incidence of feline lymphosarcoma is 416 per 100,000 cats but other studies suggest that it may be double that figure.1,2

Age incidence is inconsistent, however a survey of 26 cats at the University of Georgia over a six year period showed the following: 50% of those infected were 1–5 years; 36% were 4–8 years; and 14% were greater than 9 years. Fifty percent were male and fifty percent female, though other studies have shown males to have a three times greater risk. Siamese cats are reported to have a higher incidence than other breeds.5

Lymphosarcoma can affect any organ of the body with clinical signs dependent on the area of involvement. There are four main clinical manifestations of lymphosarcoma: 1) mediastinal; 2) alimentary; 3) multicentric; and 4) leukemic.1,2,3,4,5

Mediastinal lymphosarcoma primarily involves the thymus, sternum and anterior mediastinal lymph nodes, and often causes pleural effusion. More advanced lesions involve perihilar lymph nodes and lung parenchyma. The thoracic mass may become enlarged, compress the trachea and esophagus, and result in dyspnea, coughing, choking, and dysphagia. This form is more common in young cats, 1–2 years old. Radiographically, a widened anterior mediastinum may be present; but visualization of thoracic structures may be obscured by pleural effusion. The trachea is usually deviated dorsally. Diagnosis is made by thoracentesis with microscopic observation of large numbers of immature or abnormal lymphocytes in the pleural fluid.

In alimentary lymphosarcoma the major lesions are in the GI tract and mesenteric lymph nodes with infiltration of liver and spleen common. Single or multiple mesenteric lymph nodes are frequently enlarged, and the stomach or intestines may be diffusely thickened or contain a single segmental mass. The terminal ileum is a frequent primary site. Bone marrow infiltration may also be seen. Clinical signs usually are those of a digestive disturbance, i.e., diarrhea, constipation, and anorexia. Palpation of firm, painless enlargments in the midabdomen is a major finding.

Multicentric lymphosarcoma is a disseminated form seen in a small number of cats and is characterized by bilateral enlargement of superficial lymph nodes and variable infiltration of organs such as liver, spleen, kidneys, lungs, myocardium, GI tract, eye, skin, spinal cord, and bone marrow. Splenomegaly, hepatomegaly, and enlargement of kidneys are common. Symptoms are variable and related to the organs involved. Renal infiltration with neoplastic cells is frequently seen. The lesions may be unilateral or bilateral and clinical signs are associated with renal failure. Uremia is usually present. Nonspecific signs include fever, anemia, stomatitis, upper respiratory infections, and weight loss. Hematologic involvement is seen in about 15% of the cases of lymphosarcoma. In these cases anemia, leukopenia, and thrombocytopenia may develop.

A final classification is that of true leukemia. Cats with solid tumors of lymphosarcoma usually have normal blood counts. In recent years there has been an increase in incidence of primary leukemia involving blood and bone marrow without solid tumors. Clinical signs are vague and include lethargy, anorexia, weight loss, anemia, and sometimes fever. Diagnosis is made by blood examination. Anemia is usually nonregenerative and total WBC counts are usually normal or below normal although some cases do occur with WBC counts greater than 400,000.3 Neutropenia often is present and predisposes to infection. Total lymphocyte count may be
high or low with variable numbers of abnormal cells. Platelet numbers are variable.

Persistence of immature lymphocytes in the blood, especially in anemic cats, warrants bone marrow examination. Normal cats have less than 20% normal lymphocytes (most have less than 10%). A positive diagnosis can be made if greater than 40% of the nucleated marrow cells are lymphocytes and the majority of these are prolymphocytes or blasts.

Cats in the preleukemic state have vague or occasionally no signs of illness except a mild anemia (PCV of 25–30) with a few atypical lymphocytes. No specific treatment is indicated except to treat any coexisting problem such as infection. These cats should be closely monitored for leukemia or other diseases.

FeLV also causes immunosuppression with increased susceptibility to various infections resulting from cell mediated and humoral immunodeficiency. Because of this many adult cats with persistent FeLV infections have chronic or recurrent disease problems. A high incidence of FeLV infection has been observed in cats with infectious peritonitis, infectious anemia, toxoplasmosis, stomatitis, and respiratory disease, evidently because the virus lowers their resistance. Poor response to treatment may result in chronic illness. Glomerulonephritis is suspected to be caused by formation of FeLV antigen-antibody complexes in renal glomeruli, and the virus may have a causative role in fetal absorption and abortion.

DISCUSSION

In many exposed cats a humoral antibody response suppresses development of the disease. Virus-neutralizing antibodies protect against virus infection, and antibodies against surface antigen or infected cells (feline oncornavirus-associated cell membrane antigens, or FOCMA) prevent tumor formation. These antibodies are transferred in colostrum from immune queens, thus providing temporary protection for their kittens.

The most practical means for diagnosis is the direct immunofluorescence technique which detects FeLV antigen on platelets and leukocytes in blood smears. Recently an in-hospital ELISA test for FeLV has been made commercially available to the practitioner. One report claims it is faster, more accurate, and less expensive than the FA test but it is best suited for hospitals in which several samples per week are tested for FeLV.

Two serological tests have been developed for detection of antibody to FeLV or FeLV induced antigen. The FOCMA test detects serum antibodies to new cell surface antigens induced by the virus (not the virus itself). Because FOCMA is present on the surface of FeLV transformed cells, antibodies against FOCMA are thought to protect infected cats from tumor development. Antibody to FOCMA does not react with the virus and so does not interfere with the viremia. In infected cats, high FOCMA titers have been shown to prevent lymphosarcoma development.

The virus neutralizing antibody test measures antibody to the virus envelope antigens. It is still only a research tool; if the test becomes commercially available it will be invaluable to the practitioner. By utilizing tests that detect both virus and virus-neutralizing antibodies, it will be possible to determine whether a cat is susceptible, has been previously infected, or is viremic. Knowledge of a cat's disease status will be valuable to catteries and multiple cat households as testing can be directed toward susceptible animals and not the entire population. Previously infected but recovered cats can then be kept in a breeding situation.

Even with treatment, lymphosarcoma should be considered an incurable disease at this time. Although an occasional cat will be cured, most will eventually die of the disease. Therefore, the goal of therapy is remission. But before an owner decides to treat a FeLV-infected cat, he should have an understanding of the disease, the potential danger to other cats, prognosis, potential side effects of the treatment, frequency of clinic visits, and cost. The patient should be treated on an outpatient basis, and the veterinarian must make certain that emergency care is available since serious problems may abruptly arise during the course of treatment.

If treatment of the disease is desired, further patient evaluation is necessary to determine the extent of the disease and whether secondary problems are present. Primary problems referable to organ dysfunction may include renal failure, dyspnea, vomiting, or posterior paralysis, and the clini-
cian must try to judge whether these problems would be reversible with chemotherapy.

Myelosuppressive drugs used in chemotherapy predispose the cat to infection which severely limits drug treatment. If anemia is present, myelosuppressive drugs should be used only if supportive measures including blood transfusions are available. They should also not be used if leukopenia and thrombocytopenia is present, as routine replacement of WBC’s and platelets is not practical in cats. Low neutrophil counts predispose to infection and to thrombocytopenia which, although occurring less frequently, is a grave prognostic sign. Although fever may be directly associated with lymphosarcoma, infection may be present, so urine and blood cultures should be run. Any infection should be treated aggressively with antibiotics and in the same manner it would be treated in a non-FelV infected cat. In summary, the ideal cat to treat is afebrile with normal blood parameters, no coexisting infection, and normal liver and kidney function.

The currently employed methods of therapy include surgery, irradiation, and chemotherapy. The rare solitary lymphosarcoma may be managed by localized forms of therapy such as surgical excision (followed by chemotherapy) or irradiation. Lymphoid neoplasms are very radiosensitive; but because they are generalized, radiation treatment is precluded.

Chemotherapy is divided into three stages: induction of remission, maintenance, and relapse or recurrence therapy. All currently used methods differ somewhat in each of these stages, modifications will be made as knowledge of existing drugs improves and as new drugs become available. Prednisolone, cyclophosphamide, cytosine arabinoside, and vincristine are drugs widely used to reduce tumor mass and establish clinical remission. Combination therapy with these drugs enhances their efficacy, as each drug has a different mechanism of action and different toxicity. Therefore, the effect on the malignant cell is additive while the toxicity is not. Using chemotherapeutic drugs in combination, results in the percentage and length of remission to be greater than if they were used alone.

Treatment must be aggressive, risking some side effects to obtain longer remission. Remission is achieved when clinical signs of disease have disappeared and laboratory determinations fail to reveal the presence of tumor cells, which is usually 2–6 weeks.

Patient monitoring and supportive care are important. Bactericidal antibiotics are given if fever develops, and anticancer drugs are temporarily discontinued if leukopenia or thrombocytopenia develops. Cytotoxic drugs are not indicated if leukopenia or anemia is present. In such cases prednisone and L-asparaginase are used initially until the marrow regenerates sufficiently to allow the use of cytotoxic drugs. If induction of remission cannot be achieved with the drugs listed earlier, other drugs may be used. They include vinblastine, adriamycin, chlorambucil, L-asparaginase, and bleomycin. Following induction of remission, maintenance chemotherapy is given using drugs and doses similar to induction remission, but at longer intervals.

With time, tumor cells often become resistant to the drug used in induction and maintenance therapy. Following relapse a second remission is difficult to attain; if a remission does occur, it is usually of short duration. This second remission can sometimes be achieved by using the inducing drugs at high initial dosages or by using the alternative cytotoxic drugs.

Data from Angell Memorial Animal Hospital in Boston indicates that the length of remission, using their drug schedules, varies greatly, with a median of about four months. It is not unusual for cats to do well from six to ten months, and rarely a cat will be cured. However, some cats, particularly those with leukemia, anemia, or leukopenia, may not respond. Treatment may be stopped after continuous complete remission of one year. Causes of death include relapses, anemia refractory to transfusion therapy, and infection caused by myelosuppression due to chemotherapy or direct immunosuppression of FeLV.

As far as prevention is concerned, there are no vaccines commercially available, though research on live and inactivated FeLV vaccines is being done. If FelV is a problem in a cattery, the best method to eliminate infection is to identify carriers and eradicate them. The remaining virus-negative cats should be retested at three month intervals, and after two negative tests the cattery may be free of infection. If a positive cat is going to
become negative it will most likely do so within three months, and it may be possible to isolate FeLV. Concurrently, with elimination of positive cats the premises should be rid of the virus. The virus is destroyed by 70% alcohol and most detergents and disinfectants.

In a multiple cat household, the diagnosis of one FeLV positive cat means the other cats in the house are already exposed. Therefore, elimination of this cat for the protection of others is useless unless other FeLV positive cats are also eliminated. Any FeLV positive cat should be kept indoors to protect other cats and to protect the positive cat from exposure to other infections to which he is susceptible.13

There has been considerable controversy about the potential health hazard of FeLV to man. The FeLV will grow in human cells in tissue culture; and although serological studies have shown antibodies to various FeLV associated antigens in human serum, they have indicated that there is no positive association between FeLV and leukemia in man.

There is no increased evidence of leukemia in veterinarians or in families who have owned cats with lymphosarcoma, and no instances of human leukemia have ever been traced to cats. Therefore, the decision to euthanize an animal on the basis of danger to man is unfounded and instead should be based on the type and severity of the disease, the owner's feeling toward the animal, and the animal's potential for infecting other cats.

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