東京地区の野良ネコにおける白血病ウイルス汚染状況

誌名	Japanese journal of veterinary science
ISSN	00215295
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巻/号	49巻6号
掲載ページ	p. 1162-1164
発行年月	1987年12月

Feline Leukemia Virus Infection in Street Cats in Tokyo Area

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(Received 3 October 1986/Accepted 29 July 1987)

Jpn. J. Vet. Sci. 49(6): 1162–1164, 1987

KEY WORDS: feline leukemia virus, street cat.

Feline leukemia virus (FeLV) is a horizontally transmitted RNA tumor virus known to induce lymphoma and/or leukemia in cats infected under natural conditions. Among cats infected with FeLV, only a small minority develops persistent infections that involve a continuous replication and dissemination of the virus [6]. Most rid themselves of the virus infection and tumor development, presumably in parts via the antibody responses against virus envelope glycoprotein (gp70) [8] and feline oncornavirus-associated cell membrane antigen (FOCMA) [4]. FOCMA was initially defined as an antigen detected on the cell membranes of cultured feline lymphosarcoma (FL74) cells, which produce all three subgroups (A, B and C) of FeLV, by membrane fluorescent antibody test (MFAT) using antibody present in certain cat sera [5], and involved in immunosurveillance against tumor development [3]. The correlation between development of high levels of antibodies to FOCMA and resistance to development of leukemia or lymphoma following exposure to FeLV was found [4].

In Japan, epidemiological study of FeLV infection was first carried out in pet cats of Tokyo area by detecting FeLV-p27 antigen [14]. Furthermore, Mochizuki *et al.* [15] investigated the presence of FeLV and neutralizing antibody against FeLV in plasma of cats in South-Kyushu area. Fujita *et al.* [7] also examined the existence of FeLV-p27 antigen and anti-FOCMA antibody in sera of cats in Sapporo area. In these studies, the plasma or sera tested were from cats brought to veterinary hospitals. However, the immune-status of anti-FeLV or FOCMA antibody in clinically healthy street cats in Japan has not been studied. In this paper, we report about the seroepidemiological survey of FeLV or FOCMA in street cats in Tokyo area.

The sera used were collected from cats brought in the laboratory animal centers of three medical universities located in the Tokyo district for the purpose of experimental use. Most of the cats were outbred street cats obtained from the public health center. The living environment and the FeLV-exposure history of these cats were unknown.

The antibodies against FeLV-gp70 were detected by enzyme-linked immune sorbent assay (ELISA). The FeLV collected from the supernatant of FL74 cells [18] were purified by the same method as described by Hardy [9] and gp70 was purified as described previously [17]. The ELISA was performed in the same manner as described previously using peroxidase-conjugated anti-cat goat serum (Cappel Laboratories, Inc., PA, USA) [1]. The colorimetric reaction was carried out by azinodi-(3-ethylbenzthiazoline surfonic acid) and absorbance at 405nm was measured. Sera from specific-pathogen-free or germ-free cats were used as the negative control in the ELISA and the average absorbance of these sera was 0.53±0.12 (average±SD). The average absorbance of serum-free control was 0.52±0.07 (average±SD). The sera that gave an absorbance of more than 0.77 (average of the negative control+2SD) were considered as FeLV antibody-positive. The antibody titer was designated as the reciprocal of the highest dilution of the serum that gave an absorbance of more than 0.77.

The antibody against FOCMA was examined by

Table 1. Detection of FeLV antigen and antibodies against FeLV or FOCMA in cat sera

FeLV antigen or antibody	University			Total
	Sa.	Ki.	Ke.	
FeLV-p27 antigen	5/99[a] (5.1)[b]	1/22 (4.5)	17/259 (6.6)	23/380 (6.1)
Anti-FOCMA antibody	8/99 (8.1)	1/22 (4.5)	11/324 (3.4)	20/445 (4.5)
Anti-FeLV gp70 antibody	3/59 (5.1)	0/22 (0)	18/323 (5.6)	21/404 (5.2)

a) Positive/examined.
b) %.

Table 2. Immune status of cats against FeLV and FOCMA

FeLV antigen	No. of Cats	Antibody status			
		FeLV[a](−) FOCMA(−)	FeLV[a](−) FOCMA(+)	FeLV[a](+) FOCMA(−)	FeLV[a](+) FOCMA(+)
+[b]	23(5.1)[d]	12(2.7)	1(0.2)	8(1.8)	2(0.4)
−[c]	357(80.3)	332(74.7)	16(3.6)	8(1.8)	1(0.2)
Unknown	65(14.6)	63(14.2)	0(0)	2(0.4)	0(0)
Total	445(100.0)	407(91.6)	17(3.8)	18(4.0)	3(0.6)

a) FeLV-gp70
b) Positive
c) Negative
d) %

MFAT as described previously [5]. The FL74 cells were used as target cells [18]. The FeLV-p27 antigen was detected by ELISA using Leukassay F (Pitman-Moore, Inc., NJ, USA).

The results of the detection of FeLV antigen and antibodies against FeLV gp70 and FOCMA are shown in Table 1. Twenty-three (6.1%) of the 380 cats were positive for FeLV-p27 antigen and 4.5% and 5.2% of the cats were positive against FOCMA and FeLV-gp70 antibody, respectively. Ishida *et al.* [14] reported that 3.2% of 185 healthy pet cats in Tokyo area are positive against FeLV antigen. On the other hand, we previously reported that 29% of the cats which came to the veterinary hospitals in Sapporo were positive for FeLV antigen [7]. The rate of FeLV antigen-positive cats in the present study was lower than that of diseased pet cats in our previous study but was higher than that of healthy pet cats [14]. Approximately one fourth of the street cats which brought in the Laboratory Animal Center, Teikyo University School of Medicine, fall ill during the breeding before experimental use (T. Higashihara, unpublished data). It is known that FeLV is immunosuppressive in cats and is indirectly responsible for numerous chronic secondary disease [3]. Considering these results, it may be possible to speculate that some cats were infected with FeLV at the public health center by contact with FeLV-infected cats or some virus-positive cats came from FeLV exposure environments, such as multiple cat households in which there was a history of FeLV disease. The antibody titer against FeLV-gp70 was variable. Each of the four cats had an antibody titer of either 1:160 or 1:80, eight had 1:40, and the rest five cats had antibody titers of 1:20 or 1:10. Mochizuki *et al.* [15] reported that 7.7% of 39 healthy pet cats in South-Kyushu area were positive against FeLV neutralizing antibody. The positive rate of the sera from healthy cats in the present experiment was low and the results were similar to those reported previously [15].

The immune-status of cats against FeLV gp70 and/or FOCMA are shown in Table 2. Recently, Vedbrat *et al.* [19] reported that FOCMA was identical with the gp70 of FeLV-C, that was rarely ever found in infected pet cats. In contrast, Snyder *et al.* [16] found that FOCMA was related to, but distinguishable from, FeLV-C gp70. Thus, FOCMA may be a variant of FeLV-C gp70 or a recombinant gp70 molecule [10]. However, these findings do not alter the previous conclusion that FOCMA is an FeLV-induced tumor specific antigen [10]. A high titer of FOCMA antibody is correlated with resistance to lymphoma formation, even in persistently viremic cats. Conversely, cats with lymphoma or cats never exposed to FeLV have a very low or no titers of FOCMA antibody [11, 12]. In the present study, about three fourths of the cats were negative against both FeLV-antigen and antibodies, indicating that these cats had never been exposed to FeLV. Twelve FeLV antigen-positive cats had no antibodies against FeLV gp70 or FOCMA. They are the infected cats supposed to be susceptible to lymphoma formation [3. 11]. Twenty five FeLV antigen-negative cats had antibodies against either FeLV or FOCMA or both, indicating that these cats had been exposed to the virus. Three FeLV antigen-positive cats and 17 FeLV antigen-negative cats had antibodies against FOCMA. It is known that certain cat sera react not only with FOCMA but also with FeLV antigen on FL74 cells [2]. In the present study, only three out of the 20 FOCMA antibody-positive cats had antibody against FeLV, indicating that 85% of the sera reacted specifically with FOCMA. Previously, Hardy *et al.* [13] reported that cats with FOCMA antibody of more than 1:32 were resistant to tumor formation. In the present study, the titer of anti-FOCMA antibody were rather low and no cat had an antibody titer of over 1:32. It is unknown whether the cat which had FOCMA antibody in the present study are resistant to lymphoma formation or not. Ten FeLV antigen-positive cats also had antibodies against FeLV gp70. This phenomenon might be explained by the fact that the ELISA antigen used for

detection of antibody against FeLV was gp70 whereas the antigen detected by Leukassay F was p27.

In conclusion, this study indicates that the FeLV infection is prevalent in street cats in Tokyo area. Considering immunosuppressive effects of the virus infection, more attention should be paid to the FeLV-status of the cats used for the experiments.

ACKNOWLEDGEMENTS. We thank Dr. Hisao Izawa, Department of Epizootiology, Faculty of Veterinary Medicine, Hokkaido University, for his encouragement in the course of this study. We are indebted to many veterinary students belonging to Department of Epizootiology, Faculty of Veterinary Medicine, Hokkaido University for their technical assistance during the surveillance studies.

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要　約

東京地区の野良ネコにおける白血病ウイルス汚染状況(短報)：東原朋子・前島一淑[1]・藤川勇治[2]・見上　彪(北海道大学獣医学部家畜伝染病学講座，[1]慶応大学医学部動物実験施設，[2]共立商事(株))——東京地区の野良ネコの血清を用いてネコ白血病ウイルス（FeLV）p27 抗原，FeLV gp70 ならびにネコ白血病ウイルス付随細胞膜抗原（FOCMA）に対する抗体の検出を試みた．380匹のネコのうち，23匹（6.1%）が FeLV-p27 抗原陽性であった．また，4.5%が FOCMA 抗体陽性であり，FeLV-gp70 抗体は 5.2% で陽性であった．