A Case of Feline Large Granular Lymphoma
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In feline cases of the alimentary type of malignant lymphoma, feline leukemia virus (FeLV) was often negative [6] and the neoplastic cells were disclosed to be mostly B cell origin [7]. The present report describes a FeLV-infected cat bearing an alimentary type of lymphoma with neoplastic large granular lymphocytes (LGL). These neoplastic lymphoid cells expressed neither T nor B cell surface markers and released biologically active substances, interleukin 1 (IL-1) and interleukin 3 (IL-3).

A four-year-old neutered female domestic cat was admitted to the Veterinary Hospital, Faculty of Agriculture, University of Tokyo, because of anorexia, diarrhea and weight loss. Physical examination revealed no abnormal findings such as an enlargement of superficial lymph nodes and splenomegaly. Hematological examination showed a mild leukocytosis (16000 cells/μl). Eight days after the initial admission, a marked leukocytosis (53000 cells/μl) with neutrophilia (78%) was noted. However, no leukemic cells were detected in the peripheral blood. Serum chemistries revealed elevated levels of lactate dehydrogenase (227 IU/l). The enzyme-linked immunosorbent assay (ELISA) for FeLV by using a Leukassay F kit (Pitman Moore Inc., Washington Crossing, NJ) was positive. Ascites was confirmed by abdominal radiography and aspirated for the cytological examination. Giemsa-stained smears of ascitic cells exhibited numerous abnormal mononuclear cells (Fig. 1). Most of these cells had a round or oval nucleus with prominent nucleoli and basophilic cytoplasm with several large azurophilic granules. Mitotic figures were frequently observed. By cytochemical staining, these cells were negative for peroxidase and acid α-naphthyl acetate esterase (ANAE), and positive for β-glucuronidase and succinyl dehydrogenase [11]. Six percent of ascitic cells formed E-rosettes with guinea pig erythrocytes, and only 10% were cell-surface immunoglobulin positive, suggesting that most of ascitic cells have neither feline T nor B cell surface markers. Based on these morphological and immunological findings, the neoplastic cells in ascites may be originated from feline LGL.

Furthermore, to determine whether these neoplastic cells release biologically active factors, the cells aseptically obtained from ascites were cultured in RPMI 1640 medium (Gibco; Grand Island Biological Co., NY) supplemented with 10% fetal bovine serum (Gibco) for 24 hr at 37°C in a 5% CO₂-humidified atmosphere. The resulting cell-free culture supernatants were then harvested, and tested for IL-1 and IL-3 activities by using a C3H/HeJ mouse thymocyte proliferation assay [5] and a murine IL-3 sensitive cell line (FDC-P2) cell proliferation assay [2], respectively. As shown in Fig. 2, substantial levels of both IL-1 and IL-3-like activity were detected in the culture supernatant. These results suggested that neoplastic cells by themselves have a potential to spontaneously release these biologically active factors in situ. A leukocytosis observed in this case might be due to the stimulation of bone marrow by these cytokines [1, 3].

![Fig. 1. Neoplastic mononuclear cells containing granules within the cytoplasm on a smear of ascites. Giemsa stain. ×1320.](image-url)
Fig. 2. The proliferative response of C3H/HeJ mouse thymocytes (○) and murine IL-3 sensitive cell line (FDC-P2) cells (●) in the presence of serially diluted culture supernatants of ascitic cells from the case. Each point represents the mean count per minute (cpm) of tritiated thymidine (\(^{3}H\)-Tdr) incorporation for triplicate cultures. Background incorporation was 355 cpm in a C3H/HeJ mouse thymocyte proliferation assay and 1322 cpm in a FDC-P2 cell proliferation assay, respectively.

Fig. 3. The endocrine and exocrine glands of the pancreas are almost replaced by neoplastic cells infiltrated severely. A mild proliferation of the connective tissue is noted. HE. ×30.

This cat received chemotherapy with cyclophosphamide and prednisolone under the diagnosis of malignant lymphoma. The following day after the onset of therapy, the ascitic fluid was disappeared radiographically. The patient cat, however, became suddenly depressed and died 10 days later despite of extensive supportive treatments.

At necropsy, the most prominent finding was an enlargement of the pancreas with increased solidity. Other organs including the liver, lungs, kidneys, spleen and mesenteric lymph nodes appeared intact in both color and size. Neither pleural nor abdominal masses were noted.

Histopathologically, the pancreas was replaced by proliferative neoplastic cells (Fig. 3). Neoplastic cells infiltrated severely from serosal surface to the smooth muscle layers of the large intestine (Fig. 4) and in the omentum. The Peyer’s patches were not involved in the lesion. A mild dissemination of neoplastic cells was also observed at the perivascular areas of the brain and the lamina propria of the bladder. No significant alterations were found in other organs including the bone marrow, mesenteric lymph nodes and spleen. An electron microscopic finding of neoplastic cells infiltrated in the pancreas revealed that typical cells possessed a kidney-shaped nucleus with diffuse chromatin and a single nucleolus (Fig. 5). In the cytoplasm, some electron-dense granules with a narrow halo were present. These histopathological findings suggest that the neoplastic
LGL might arise in certain small lymph nodes of the alimentary area, and disseminate to the intestinal tissue.

LGL were a major cell population responsible for natural killer (NK) activity in humans [9], and were distributed in the intestinal epithelium as well as the spleen and peripheral blood [8]. Although a few reports on feline NK cells [10] and large granular lymphoma [4] were presented, the association of feline LGL with NK activity has not been fully defined. The lymphoma cell line derived from this case has been established in our laboratory, and is now under investigation for the NK activity and lymphokine synthesis.

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REFERENCES


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ネコのlarge granular lymphomaの1例（速報）：後藤健次・辻 美保・松本安喜・恩田千景・松岡清美1）横森謙子2）・安田和雄1）・倭田好和・小野隆一郎・林 俊春2）・長谷川和彦（東京大学農学部家畜内科学教室）1）附属家畜病院，2）家畜病理学教室）——消化器症状を呈したネコ白血病ウイルス陽性ネコの膿水に，細胞質アズルー顆粒を有する幼若な単核細胞が認められ，β-glucuronidase染色陽性性T・B細胞表面形質を欠くことから，large granular lymphocyteに由来する腫瘍細胞であることが示唆された。本腫瘍細胞の培養上清中にはインターロイキン1およびインターロイキン3様活性が検出され，病理組織学的には腫瘍および大腸に腫瘍細胞の浸潤が認められた。