NOTE *Internal Medicine*

Bone Marrow Necrosis in a Cat Infected with Feline Leukemia Virus

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ABSTRACT. A one-year old castrated male cat was admitted to the hospital with vomiting and diarrhea. Laboratory examination revealed pancytopenia and positive for FeLV antigen. A bone marrow examination indicated necrosis of the nucleated cells. Based on these findings, the cat was diagnosed as bone marrow necrosis. Pancytopenia was effectively treated with corticosteroids. Re-examination of the bone marrow confirmed a recovery of normal hematopoietic cells with a infiltration of many macrophages. It is strongly suspected that the bone marrow necrosis in this case could be associated with a bone marrow suppression due to FeLV infection.—KEY WORDS: bone marrow necrosis, feline, feline leukemia virus.

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Feline leukemia virus (FeLV) is known to induce a variety of hematological abnormalities, including proliferative and depressive changes in the bone marrow cells [2, 15].

The present study documented chronological changes in the blood and bone marrow examination of a feline case with FeLV infection that showed pancytopenia and was subsequently diagnosed as having bone marrow necrosis (BMN). BMN in cats has not reported as far as authors know.

A one-year old castrated male cat was referred to the hospital because of vomiting and diarrhea. The cat had been inoculated with FVR-CP vaccine, and did not have any past medical history. A general physical examination confirmed fever (40.0°C), gingivitis, and a pyogenic ulcer in the pharynx, while a blood examination showed severe neutropenia (40/μl). Virological examination indicated the presence of FeLV antigen in peripheral blood, but feline immunodeficiency virus (FIV) antibody did not present in peripheral blood. On the fourth day after the first presentation, neutrophils were absent. Thrombocytopenia ($30 \times 10^3/\mu l$) and anemia (PCV: 24%) were also found. Reticulocytes were undetectable. Smears of bone marrow aspirates stained with Wright-Giemsa showed grayish pink colored cells, but did not show any well-defined nuclei, thus suggesting necrosis. Furthermore, absolutely no normal hematopoietic cells could be seen. A bone marrow biopsy revealed extensive necrosis, and nuclear swelling and karyolysis were found in the nucleated cells (Figs. 1, 2). In addition, no increases in fat tissue or fibroblasts were seen, thus confirming that the cat did not have aplastic anemia or myelofibrosis. Based on these findings, the cat was diagnosed as having bone marrow necrosis. The fever persisted despite repeated administration of antibiotics, begun on the initial day of the examination. Between the 6th and 10th days of the illness, dexamethasone was administered (8, 8, 4, 2 and 1 mg/head, respectively), followed by 5 mg/head of prednisolone administered every day until the 18th day of the illness. On the 7th day of the illness, the fever disappeared, and the cat regained vitality and appetite. The results of a blood examination performed on the 11th day of the illness confirmed anemia (PCV: 19%) and neutropenia (850/μl), and a normal platelet count. On the 18th day of the illness, an increase in neutrophils ($3.2 \times 10^3/\mu l$) and the presence of reticulocytes were confirmed. Large quantities of dexamethasone were administered between the 19th and 23rd days of the illness in the same manner as before. The results of a blood examination conducted on the 35th day of the illness were as follows: PCV level of 28%, neutrophil count of $3.6 \times 10^3/\mu l$, and a normal platelet count. The PCV level increased significantly from this point on, and elevated to 35% on the 47th day of the illness and 43% on the 95th day of the illness (Fig. 3). The results of a bone marrow aspiration performed on the 22nd day showed necrotic cells and many phagocytic macrophages (Fig. 4). The results of a bone marrow biopsy also showed the infiltration of macrophages in necrotic tissue, and an insular mass of normal hematopoietic cells was found in some areas (Fig. 5). The results of a separate

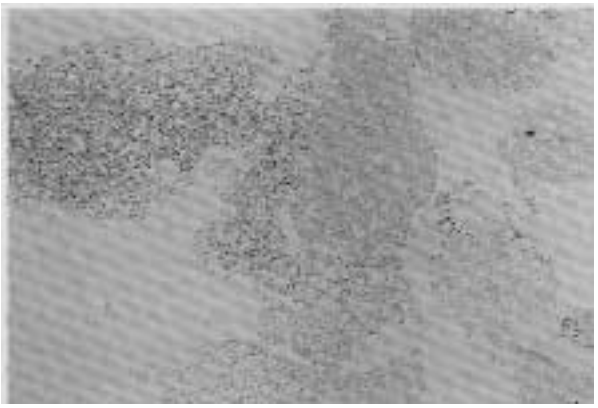

Fig. 1. Lower power view of histological findings of bone marrow in a cat with BMN on the 1st day. H. E. stain × 40. Extensive bone marrow necrosis was seen.

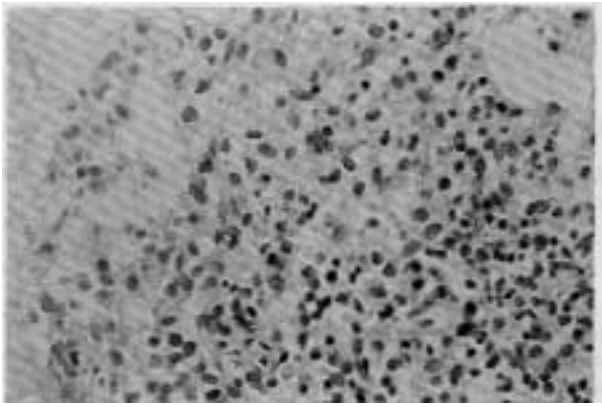

Fig. 2. Higher power view of histological findings of bone marrow in a cat with BMN on the 1st day. H. E. × 400. Imhibition of nuclei and karyolysis were seen.

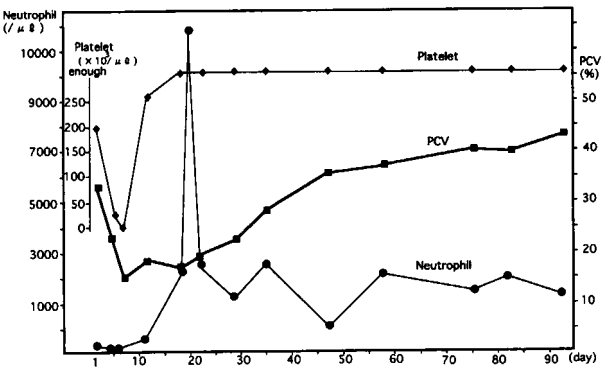

Fig. 3. Time course of hematological changes in a cat with BMN. (PCV, Neutrophils, Platelets)

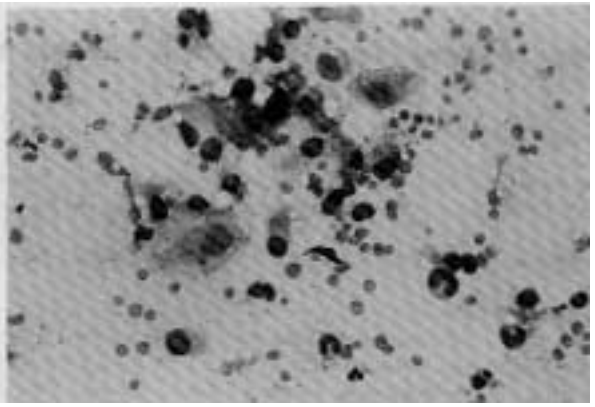

Fig. 4. Bone marrow findings by aspiration on the 22nd day. Wright-Giemsa stain × 400.

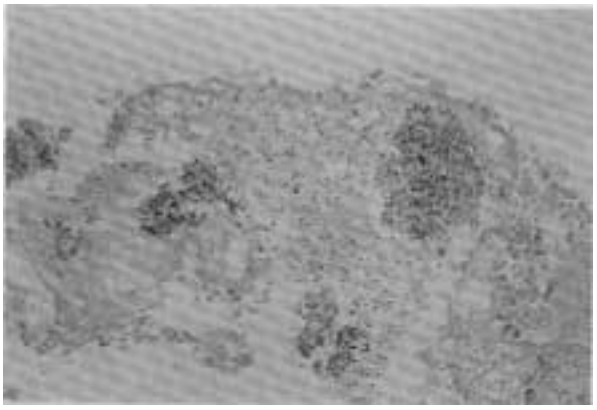

Fig. 5. Histological findings of bone marrow on the 22nd day. H. E. × 100. Macrophages were seen in the area of necrosis and normal hematopoietic tissue were observed partially.

bone marrow aspiration performed on the 47th day also showed multiple macrophages, and a bone marrow biopsy confirmed hemopoietic regions accompanied by fatty tissue (Fig. 6). An additional bone marrow aspiration was performed on the 95th day of the illness. The results were as follows: no necrotic cells nor any increased macrophage could be seen; hyperplasia of erythroblasts and mild hypoplasia of granulocytic cells were found; the number of megakaryocyte was normal; and no morphological abnormalities were detected with various cells (Fig. 7).

Pancytopenia can occur in cats with FeLV infection when accompanied with illnesses such as acute leukemia, myelodysplastic syndrome (MDS), aplastic anemia, myelofibrosis, and panleukopenia-like syndrome [2, 15]. In acute leukemia or MDS, the bone marrow cells are hyperplastic or nomoplastic with increase number of blast cells and dysplastic changes in these cells are also observed. In aplastic anemia bone marrow cells are hypoplastic or aplastic with increase of fat tissue and with slight infiltration of lymphocytes and plasmacytes. An increase of fibroblasts is characteristic to myelofibrosis. However, necrotic hematocytes are generally absent in these diseases. Since the cat in this study showed significantly different clinical symptoms from the other hematopoietic disorders, it was diagnosed to be BMN similar to that in human.

Human BMN is sometimes detected by a postmortem examination, and is rarely diagnosed prior to death [4, 10]. Human BMN was confirmed mostly in patients with malignant diseases such as hematological neoplasias (lymphoma, acute and chronic leukemia) or intramedullary metastasis of malignant carcinoma. It was also reported in patients with sepsis or sickle cell anemia [5, 6, 10, 11, 13]. The main clinical symptoms of bone marrow necrosis are fever and bone pain, and the laboratory examination indicated a variety of findings including anemia, pancytopenia, hypercalcemia and leukoerythroblastosis [3, 5, 6, 8]. However, no reports on BMN in animals are found in the literature.

As we previously observed a similar feline case of BMN, we have strongly suspected that BMN could be associated with FeLV infection. The onset mechanism of BMN is not clearly known, but it has been suggested that occlusion of medullary microcirculation or necrosis inducers may play a

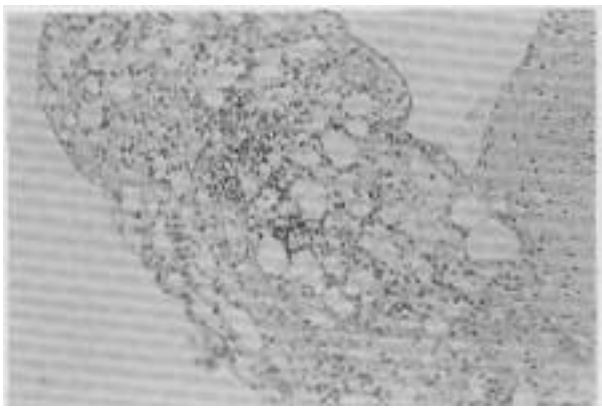

Fig. 6. Histological findings of bone marrow on the 47th day. H. E. × 100. Fat tissue increased with hematopoiesis.

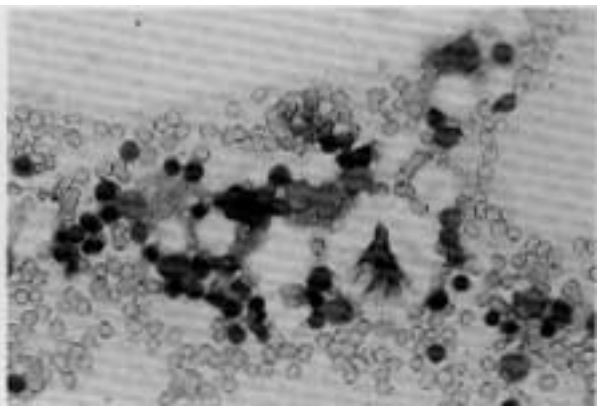

Fig. 7. Bone marrow findings by aspiration on the 95th day. Wright-Giemsa stain × 400. Normal hematopoiesis was seen with slight hyperplasia of erythroid cells.

role in this disease [1, 8, 14]. Knupp *et al.* demonstrated that the concentration of tumor necrosis factor (TNF) in the blood of cancer patients with BMN was higher than that of cancer patients without BMN, which led them to conclude that TNF is involved in the onset of BMN [9]. Furthermore, TNF has been shown to be involved in erythroid hypoplasia caused by the FeLV subgroup C [7], suggesting the involvement of TNF in bone marrow suppression. This result suggested that TNF may induces bone marrow necrosis in cats infected with FeLV. The pathogenesis of feline BMN should be investigated further in relation with FeLV infection.

The cat in this study had a FeLV infection, but no neoplastic diseases such as lymphoma or leukemia. The prognosis of this cat was good. The prognosis for human BMN is known to be affected not by the severity of necrosis but by the type of underlying diseases [11]. The prognosis is good for human BMN accompanying infections or sickle cell anemia, but poor when accompanied by malignant disease such as lymphoma, leukemia, and intramedullary metastases of neoplasms [5, 6, 8, 11, 12, 14].

REFERENCES

1. Conrad, M. E. and Carpenter, J. T. 1979. *Am. J. Hematol.* 7: 181–189.
2. Cotter, S. M., Hardy, W. D. Jr. and Essex, M. 1975. *J. Am. Vet. Med. Assoc.* 166: 449–454.
3. Dunn, P., Shin, L. Y., Liaw, S. J. and Sun, C. F. 1993. *J. Formos. Med. Assoc.* 92: 1107–1110.
4. Dzieciol, j., Kemona, A., Sulik, M., Bernaczyk, A., Sulkowski, S. and Brykalska, A. 1989. *Pathol. Pol.* 40: 211–218.
5. Godeau, B., Bachir, D., Randrianjohanny, A., Jouault, H., Galacteros, F., Portos, J. L. and Schaeffer, A. 1994. *Rev. Med. Intern.* 15: 25–29.
6. Hamidou, M., Rigal-Huguet, F., Moreau, A., Ducloux, J. M., Accard, F., Dupas, B. and Grolleau, J. Y. 1993. *Rev. Med. Intern.* 14: 958.
7. Khan, K. N., Kociba, G. J., Wellman, M. L. and Reiter, J. A. 1992. *In Vitro Cell Dev. Biol.* 28: 260–266.
8. Kiraly, J. F. and Wheby, M. S. 1976. *Am. J. Med.* 60: 361–368.
9. Knupp, C., Pekala, P. H. and Cornelius, P. 1988. *Am. J. Hematol.* 29: 215–221.
10. Leyssen, M. H. and Verwilghen, R. L. 1979. *Clin. Lab. Haematol.* 1: 197–202.
11. Maisel, D., Lim, J. Y., Pollock, W. J., Yatani, R. and Liu, P. I. 1988. *Ann. Clin. Lab. Sci.* 18: 109–115.
12. Moore, J., Ma, D. D. and Concannon, A. 1998. *Pathology* 30: 318–320.
13. Ranaghan, L., Morris, T. C., Desai, Z. R. and Markey, G. M. 1994. *Am. J. Hematol.* 47: 225–228.
14. Scudla, V., Dusek, J., Macak, J., Zivna, J., Myslivecek, M. and Indrak, K. 1989. *Neoplasma* 36: 603–610.
15. Shelton, G. H. and Lihenberger, M. L. 1995. *Seminars in Vet. Med. and Surg. (Small Anim.)* 10: 220–233.