

CASE REPORT

Acute erythroid leukemia with probable splenic involvement initially interpreted as large-cell lymphoma in a feline leukemia virus-negative Persian cat

Sung-Hyun Han^{1,3}, Dong-Jin Chae^{2,3} and Kun-Ho Song^{3*}

¹Time Animal Medical Center, Daejeon, Republic of Korea.

²Department of Animal Health Management, Woosong University, Daejeon, Republic of Korea.

³Department of Veterinary Medicine, Chungnam National University, Daejeon, Republic of Korea.

*Corresponding author
songkh@cnu.ac.kr

Received: 20.07.2026

Accepted: 24.09.2026

Published: 08.10.2026

ABSTRACT. A FeLV-negative Persian cat with severe non-regenerative anemia had a splenic round-cell neoplasm initially interpreted as large-cell lymphoma. CD3/PAX5 immunohistochemistry did not support conventional lymphoma, and bone marrow findings favored acute erythroid leukemia (AML-M6) with probable splenic involvement. The cat died 53 days after presentation, despite receiving cytarabine treatment.

Keywords: Acute erythroid leukemia, Feline leukemia virus, Bone marrow biopsy, Splenic involvement, Immunohistochemistry

INTRODUCTION

Acute erythroid leukemia (AML-M6) is a subtype of acute myeloid leukemia characterized by the neoplastic proliferation of erythroid precursors and blast cells. Feline AML is uncommon, accounting for 5 of 152 (3.3%) feline bone marrow samples in a retrospective study (Turinelli & Gavazza, 2018). In another study of 107 feline acute leukemias, 31 (29.0%) were erythroid leukemias, including 21 AML-M6 cases (Jain, 1993). Affected cats may exhibit lethargy, anorexia, severe non-regenerative anemia, and cytopenia (Chimenes *et al.*, 2022; Lim *et al.*, 2025; Park *et al.*, 2022). Historically, 60–80% of feline myeloid leukemias have been reported to be feline leukemia virus (FeLV)-antigen-positive (Tagawa *et al.*, 2020). Nevertheless, FeLV-negative AML, including acute erythroid and monoblastic leukemia, has been documented (Lim *et al.*, 2025; Suzuki *et al.*, 2021; Tagawa *et al.*, 2020). The etiology of FeLV-negative feline AML remains poorly understood. Diagnosis requires the integration of peripheral blood findings, bone marrow evaluation, and, when necessary, lineage-specific ancillary testing (Lim *et al.*, 2025; Silva *et al.*, 2022). Splenic involvement can complicate the diagnosis when poorly differentiated round-cell morphology overlaps with lymphoma (Lim *et al.*, 2025; Prihirunkit *et al.*, 2008). This report describes the clinicopathological findings, diagnostic process, treatment, and outcome of a FeLV-negative Persian cat with AML-M6 and probable splenic involvement, initially interpreted as large-cell lymphoma.

CASE PRESENTATION

Clinical history and examination

A 10-year-old castrated male Persian cat presented with a 2-day history of tachypnea, lethargy, and anorexia. Initial complete blood count revealed severe microcytic, non-regenerative anemia (Hct, 6.4%; absolute reticulocyte count, $18.1 \times 10^9/L$), leukocytosis with mild neutrophilia, lymphocytosis, monocytosis, and a platelet count within the reference interval. Serum biochemistry revealed azotemia (BUN, 74.55 mg/dL; creatinine, 2.82 mg/dL) and mild hyperbilirubinemia (1.56 mg/dL) (Table 1). Following transfusion and supportive treatment, HCT increased to 19.5% on day 1. By day 2, BUN had decreased to 18.15 mg/dL and creatinine to 1.49 mg/dL (Table 1). Serum amyloid A decreased from 30 µg/mL on Day 0 to 6.7 µg/mL on Day 3 and 5 µg/mL on Day 4, after a transient increase to 35 µg/mL on Day 2. Total bilirubin peaked at 7.41 mg/dL on day 2 and declined to 0.59 mg/dL by day 14 (Table 1). Concurrent gallbladder sludge with mild wall thickening and later concern for hepatic lipidosis suggested a potentially multifactorial cause, although the etiology of hyperbilirubinemia was not established.

Diagnostic tests

Abdominal ultrasonography revealed mild-to-moderate splenomegaly with a homogeneous echotexture and an enlarged, hypoechoic, rounded splenic lymph node (7.1 × 7.4 mm). Immunochromatographic tests for FeLV anti-

Table 1.
Selected serial hematologic and serum biochemical findings during the clinical course

Major clinical event	Initial presentation (day 0)	Post-transfusion (day 1)	Supportive treatment (day 2)	Post-splenectomy (day 8)	Chlorambucil initiated (day 14)	Before cytarabine treatment (day 33)	After cytarabine treatment (day 46)
HCT (%)	6.4	19.5	19.2	24.8	21.9	12.5	16.2
WBC (x10 ⁹ /L)	31.38	18.96	8.97	12.44	32.67	12.79	19.68
NEU (x10 ⁹ /L)	19.4	13.81	5.96	8.74	25.23	6.32	13.67
LYM (x10 ⁹ /L)	7.48	3.46	1.66	1.85	4.43	2.63	2.33
MONO (x10 ⁹ /L)	4.41	1.67	1.29	1.64	2.61	3.28	3.17
BUN (mg/dL)	74.55	56.48	18.15	14.83	-	26.93	-
Creatinine (mg/dL)	2.82	2.04	1.49	1.40	-	1.26	-
Total bilirubin (mg/dL)	1.56	1.04	7.41	1.24	0.59	0.37	-

Hct, hematocrit; WBC, white blood cell count; NEU, neutrophils; LYM, lymphocytes; MONO, monocytes; BUN, blood urea nitrogen; –, not measured.

gens and feline immunodeficiency virus (FIV) antibodies were negative. PCR testing for feline anemia-associated infectious agents, including FeLV, FIV, and vector-borne pathogens, yielded negative results. Splenectomy and full-thickness ileal and jejunal biopsies were performed on day 6. The cat was discharged on day 11 with an Hct of 21.8%. On day 14, splenic histopathology revealed diffuse infiltration by malignant round cells with scant cytoplasm, large nuclei, and high mitotic activity, initially interpreted as large-cell lymphoma (Figure 1A). Toluidine blue staining did not reveal any mast cell tumors (Figure 1B). Intestinal biopsies revealed mild chronic lymphoplasmacytic enteritis and muscular hypertrophy without evidence of intestinal lymphoma or splenic neoplasm extension.

Differential diagnosis and initial treatment

Primary splenic lymphoma with possible bone marrow involvement was initially considered the most likely diagnosis for this patient. Based on this interpretation, a single dose of chlorambucil (20 mg/m², PO) was administered on day 14 pending further evaluation.

Definitive diagnosis

On day 15, splenic immunohistochemistry for CD3 and PAX5 was performed to assess the lineage. The neoplastic cells were negative for both markers, failing to support the diagnosis of conventional T- or B-cell lymphoma (Figure 1C and 1D). Bone marrow aspiration and core biopsy were then performed because of persistent non-regenerative anemia and suspected hematopoietic neoplasia. The aspirate was hemodilute with poor particle recovery, and immature round cells overlapped morphologically with rubriblasts and prorubricytes, precluding a definitive lineage assignment (Figure 2A). Core biopsy revealed hypercellular marrow with erythroid predominance and dysplasia, in-

creased iron stores, absent megakaryocytes, and approximately 50% blasts (Figure 2B). Blasts and erythroid precursors comprised approximately 80% of the total nucleated cells. These findings supported acute erythroid leukemia, favoring AML-M6. As the erythroid lineage was not directly confirmed in the spleen, the splenic lesion was interpreted as probable leukemic involvement.

Treatment and outcome

Despite transfusions and supportive treatment, Hct declined to 12.5% by day 33 (Table 1). Before cytarabine treatment, the poor prognosis and limited evidence for treatment efficacy were discussed with the owner, and euthanasia was discussed as an option if clinical deterioration or unacceptable quality of life occurred. Cytarabine was administered on days 34–37 at 150 mg/m² as a 12-h constant-rate infusion once daily. No sustained hematologic response occurred; by day 46, the Hct was 16.2%, with recurrent leukocytosis and neutrophilia (Table 1). The cat was found dead at home on day 53, and necropsy was not performed.

DISCUSSION & CONCLUSION

This case highlights a diagnostic pitfall in which probable splenic involvement by acute erythroid leukemia was initially misdiagnosed as large-cell lymphoma. Poorly differentiated hematopoietic neoplasms may exhibit overlapping round-cell morphology, limiting lineage assignment based on morphology alone (Lim et al., 2025; Suzuki et al., 2021). CD3/PAX5 negativity weakened the interpretation of conventional T- or B-cell lymphoma but did not directly confirm erythroid origin. Bone marrow biopsy provided key evidence, with erythroid dysplasia, blast expansion, and marked erythroid predominance supporting AML-M6. Therefore, the splenic lesion was considered more like-

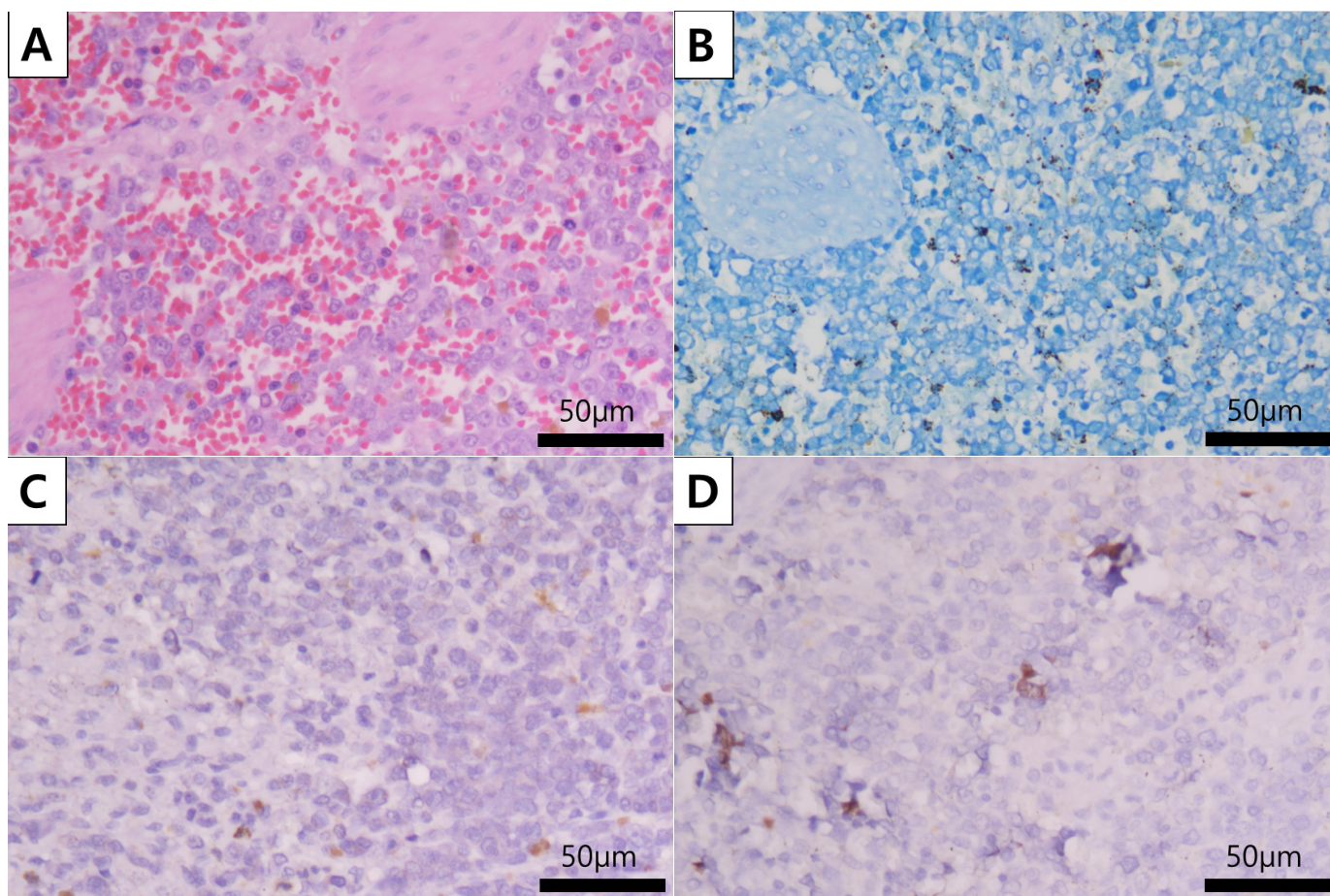


Figure 1.

Histopathological and immunohistochemical findings of the splenic lesion. A) Hematoxylin and eosin (H&E) staining showing diffuse infiltration of malignant round cells (x400); B) Toluidine blue staining did not reveal metachromatic granules in the neoplastic cells, making a mast cell tumor unlikely (x400); C) IHC for CD3 showed that the neoplastic round cells were negative for CD3, failing to support the diagnosis of T-cell lymphoma (x400); D) IHC for PAX5 showed that the neoplastic round cells were negative for PAX5, failing to support the diagnosis of B-cell lymphoma (x400).

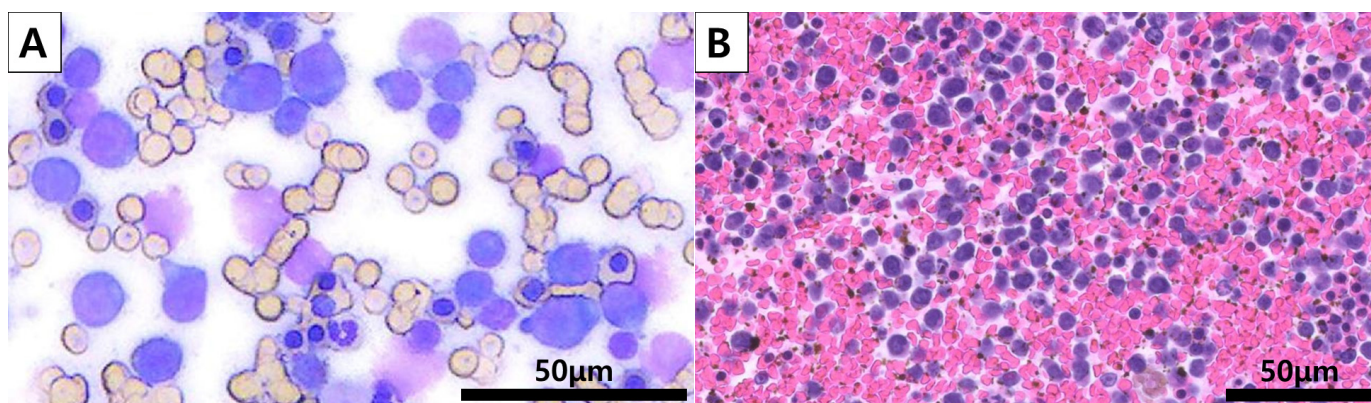


Figure 2.

Bone marrow aspirate cytology and biopsy were performed. A) Aspirate cytology showing numerous immature round-to-blast-like cells in a hemodiluted background. These cells showed morphological overlap with erythroid precursors, including rubriblasts and prorubricytes, limiting definitive lineage assignment by cytology alone (x1000). B) Bone marrow biopsy revealed a hypercellular marrow with a dense population of immature hematopoietic cells. Histopathological evaluation identified erythroid dysplasia, absent megakaryocytes, approximately 50% blastic cells, and marked erythroid predominance, supporting acute myeloid leukemia of erythroid origin, favoring AML-M6 (x1000).

ly to be leukemic involvement than primary splenic lymphoma with marrow infiltration. Splenic involvement has been documented in feline acute erythroid leukemia. In one pathological series, splenic hematopoietic involvement was identified in six of seven evaluable cats (85.7%), with additional involvement of the lymph nodes, liver, and kidneys (Tochetto et al., 2011). In a retrovirus-negative cat with AML-M6Er, neoplastic erythroid precursors were identified in the spleen and splenic lymph nodes and subsequently shown to infiltrate the splenic red pulp and vascular structures (Suzuki et al., 2021). These findings suggest that splenic lesions may represent extramedullary dissemination of marrow-derived neoplastic cells, although the frequency, timing, and prognostic significance of splenic involvement remain poorly defined in the literature. In the present case, the splenic lesion preceded the definitive bone marrow diagnosis and initially favored lymphoma. In retrospect, the combination of persistent severe non-regenerative anemia and a poorly differentiated splenic round-cell neoplasm warranted consideration of a marrow-derived hematopoietic neoplasm in addition to lymphoma. When lineage is uncertain, the integration of peripheral blood findings, bone marrow evaluation, and lineage-specific ancillary testing should ideally precede lymphoma-directed chemotherapy when clinically feasible. FeLV infection has been associated with feline hematopoietic neoplasia; however, FeLV-negative acute myeloid and erythroid leukemias have also been reported (Lim et al., 2025; Tagawa et al., 2020). FeLV/FIV coinfection has been associated with an increased occurrence of leukemia in cats (Mello et al., 2023), although an independent etiological role of FIV in feline AML has not been established. Endogenous FeLV-related retroviral elements are inherited components of the feline genome and can recombine with exogenous FeLV, potentially influencing viral tropism and pathogenicity (Canto-Valdés et al., 2023). Nevertheless, their direct contribution to FeLV-negative AML remains unknown; therefore, the etiology in the present case could not be determined. Age and breed predispositions for feline AML-M6 also remain poorly defined. In one study, five of ten affected cats were 10–14 years old, whereas only one was Persian (Tochetto et al., 2011). Thus, the age of the present cat is consistent with previously reported older cases, but no Persian breed predisposition can currently be inferred. Feline AML generally carries a poor prognosis, although reliable median survival data are unavailable because published treatment outcomes are largely limited to individual case reports. Reported survival times include 67 days for AML-M6Er treated with high-dose cytarabine and approximately 95–97 days for other AML subtypes (Lim et al., 2025; Mashita et al., 2006; Park et al., 2022). The 53-day clinical course and absence of a sustained response to cytarabine in this cat were consistent with the aggressive clinical behavior reported for feline AML. The principal limitation of this study was the lack of direct confirmation of erythroid lineage in the splenic lesion using CD71 or

other erythroid-lineage markers (Suzuki et al., 2021). PARR and flow cytometry were also not performed; therefore, concurrent splenic lymphoma could not be completely excluded. Nevertheless, the CD3/PAX5-negative splenic round-cell population, together with the marrow findings favoring AML-M6, made probable leukemic splenic involvement the more likely interpretation. The integration of splenic and marrow findings shifted the diagnosis from presumed splenic large-cell lymphoma with possible marrow involvement to AML-M6 with probable splenic involvement.

DECLARATIONS

Competing Interests

The authors declare that they have no competing interests.

Ethics Statement

Ethical approval was not required for this study because it describes a single privately owned animal that underwent diagnostic and therapeutic procedures as part of routine clinical care, with no procedures performed solely for research purposes. Written informed consent was obtained from the owner for the publication of case details and accompanying images.

Author Contributions

Conceptualization and Writing – Original Draft: DC, SH, Investigation and Data Curation: SH, DC, Supervision and Writing – Review & Editing: KS, DC. All the authors approved the final manuscript.

Funding

This work was supported by the Rural Development Administration, Republic of Korea (grant number RS-2023-00231965).

REFERENCES

- Canto-Valdés, M. C., Bolio González, M. E., Acevedo-Jiménez, G. E., & Ramírez Álvarez, H. (2023). What role do endogenous retroviruses play in domestic cats infected with feline leukaemia virus? *New Zealand Veterinary Journal*, 71(1), 1–7. <https://doi.org/10.1080/00480169.2022.2131648>
- Chimenes, N. D., Caramalac, S. M., Castilho, M. O., Gazzzone, A. C., Pupin, R. C., Palumbo, M. I. P., & Babo-Terra, V. J. (2022). Acute erythroid leukemia in a cat infected with feline leukemia virus. *Acta Scientiae Veterinariae*, 50(Suppl. 1), 832. <https://doi.org/10.22456/1679-9216.120852>
- Jain, N. C. (1993). Classification of myeloproliferative disorders in cats using criteria proposed by the Animal Leukaemia Study Group: A retrospective study of 181 cases (1969–1992). *Comparative Haematology International*, 3, 125–134. <https://doi.org/10.1007/BF00186096>
- Lim, G.-H., Kim, S.-H., Ryu, M.-O., An, J.-H., Go, D.-M., Yang, Y., Kim, D.-Y., Kim, Y., Youn, H.-Y., & Seo, K.-W. (2025). A rare case of acute erythroid leukemia (AML M6-Er) with pleural metastasis and malignant pleural effusion in a cat. *Journal of Veterinary Medical Science*, 87(6), 634–639. <https://doi.org/10.1292/jvms.24-0340>
- Mashita, T., Shimoda, T., Yoshioka, H., Takahashi, Y., & Mitsuda, M. (2006). A cat with acute myeloblastic leukemia without maturation (M1) treated with combination chemotherapy. *Journal of Veterinary Medical Science*, 68(1), 97–101. <https://doi.org/10.1292/jvms.68.97>
- Mello, L. S. de, Ribeiro, P. R., Almeida, B. A. de, Bandinelli, M. B., Sonne, L., Driemeier, D., & Pavarini, S. P. (2023). Diseases associated with feline leukemia virus and feline immunodeficiency virus infection: A retrospective study of 1470 necropsied cats (2010–2020). *Comparative Immunology, Microbiology and Infectious Diseases*, 95, 101963. <https://doi.org/10.1016/j.cimid.2023.101963>
- Park, D. S., Lee, J., Song, K.-H., & Seo, K. W. (2022). Treatment of acute erythroleukaemia with high-dose cytarabine in a cat with feline leukaemia virus infection. *Veterinary Medicine and Science*, 8(1), 9–13.

- <https://doi.org/10.1002/vms3.646>
- Prihirunkit, K., Narkkong, N.-A., & Apibal, S. (2008). Acute monoblastic leukemia in a FeLV-positive cat. *Journal of Veterinary Science*, 9(1), 109–111. <https://doi.org/10.4142/jvs.2008.9.1.109>
- Silva, T. P. da, Zanfagnini, L. G., Oliveira, A. C. de, Ribeiro, D. C., Oliveira, L. G. de, Silva, P. R. R., Messias, C. T., & Pacheco, A. D. (2022). Myelodysplastic syndrome progression to acute myeloid leukemia in a cat FeLV seroreactive. *Acta Scientiae Veterinariae*, 50(Suppl. 1), 795. https://www.ufrgs.br/actavet/50-suple-1/CR_795.pdf
- Suzuki, S., Ogino, N., Mitsui, I., Ito, H., & Kariya, T. (2021). Anti-CD71 antibody immunohistochemistry in the diagnosis of acute myeloid leukemia, subtype acute erythroid leukemia with erythroid dominance (AML M6-Er), in a retrovirus-negative cat. *Journal of Veterinary Diagnostic Investigation*, 33(1), 87–94. <https://doi.org/10.1177/1040638720973403>
- Tagawa, M., Shimbo, G., Watanabe, K.-I., Horiuchi, N., Kobayashi, Y., Maezawa, M., Matsumoto, K., & Miyahara, K. (2020). Acute monoblastic leukemia in a feline leukemia virus-negative cat. *Journal of Veterinary Medical Science*, 82(7), 1000–1005. <https://doi.org/10.1292/jvms.20-0157>
- Tochetto, C., Souza, T. M., Barros, C. S. L., & Figuera, R. A. (2011). Epidemiological, clinical, hematological, and pathological aspects of acute erythroid leukemia (AML M6) in cats. *Pesquisa Veterinária Brasileira*, 31(7), 610–619. <https://doi.org/10.1590/S0100-736X2011000700011>
- Turinelli, V., & Gavazza, A. (2018). Retrospective study of 152 feline cytological bone marrow examinations: Preliminary classification and ranges. *Journal of Feline Medicine and Surgery*, 20(12), 1158–1168. <https://doi.org/10.1177/1098612X18757602>