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Olgu Sunumu / Case Reports

A Case of Acute Lymphoblastic Leukemia in a Cat

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Abstract: This study aimed to provide information about the cytology results, clinical process, and treatment protocol of ALL diagnosed in biopsy samples taken from the lymph nodes and peripheral blood smears of a cat with feline leukemia virus infection (FeLV). The cat showed clinical signs such as enlarged mandibular lymph nodes, swelling in the frontal region of the head, ulceration and gingivitis in the oral cavity, inflammation of the anal sacs, diarrhoea and recurrent vomiting. In the haematological evaluation performed on the first day of admission to the clinic, it was found that the total WBC values could not be measured using the haematology device. Furthermore, biochemical abnormalities, including hyperproteinemia (9.5 g/dl), hyperalbuminaemia (4.08 g/dl), hypernatraemia (241.7 mEq/L) and hyperkalaemia (8.09 mEq/L), were detected in this case report. In addition, neurological findings such as keratitis, tongue paralysis and neurogenic bladder, which were not previously reported in FeLV-infected cats, were detected and reported. Despite the administration of appropriate treatment protocols, the cat survived for approximately three months following the diagnosis of the disease, a complete recovery could not be achieved due to complications. Consequently, it is crucial to implement preventive measures against FeLV infections, given the variable prognosis of the disease. This hematopoietic disease, which is not frequently encountered in cats, was prepared with the belief that it would be useful to veterinarians and is the first report of acute lymphoblastic leukemia in cats in Türkiye.

Keywords: Acute lymphoblastic leukemias, Chemotherapy treatment, FeLV, Hematopoietic neoplasm

Bir Kedide Akut Lenfoblastik Lösemi Olgusu

Özet: Bu çalışmada, kedi lösemi virüsü enfeksiyonu (FeLV) tanısı konulan bir kedinin lenf düğümlerinden alınan biyopsi örnekleri ve periferik kan smear örneklerinde teşhis edilen ALL'nin sitoloji sonuçları, klinik süreci ve tedavi protokolü hakkında bilgi verilmesi amaçlandı. Kedide mandibular lenf nodlarında büyüme, başın frontal bölgesinde şişlik, ağız boşluğu içinde ülserasyon ve gingivitis, anal keselerde yangı, ishal ve tekrarlayan kusma gibi klinik bulgular gözlendi. Kliniğe getirildiği ilk gün yapılan hematolojik değerlendirmede hematoloji cihazı kullanılarak total WBC değerlerinin ölçülemediği tespit edildi. Ayrıca bu olgu sunumunda hastalık sürecinde hiperproteinemi (9.5 g/dl), hiperalbüminemi (4.08 g/dl), hipernatremi (241.7 mEq/L) ve hiperkalemi (8.09 mEq/L) gibi biyokimyasal değişiklikler belirlendi. Ek olarak FeLV ile enfekte kedilerde daha önce bildirilmeyen keratit, dil felci ve nörojenik mesane gibi nörolojik bulgular tespit edilerek raporlandı. Kedi uygun tedavi protokolleri ile yaklaşık 3 ay kadar hayatta tutuldu fakat komplikasyonlar nedeniyle tam bir iyileşme sağlanamadı. Sonuç olarak hastalığın değişken prognozu dikkate alındığında, birincil olarak FeLV enfeksiyonlarına karşı koruyucu önlemlerin alınması önem arz etmektedir. Kedilerde sık rastlanmayan bu hematopoietik hastalık, veteriner hekimlere faydalı olacağı düşüncesiyle hazırlanmış olup, Türkiye'de kedilerde akut lenfoblastik löseminin ilk raporudur.

Anahtar Kelimeler: Akut lenfoblastik lösemi, FeLV, Hematopoietik neoplazm, Kemoterapi tedavisi

1. Introduction

Acute lymphoblastic leukemia (ALL) is characterized by the aggressive proliferation of immature and inadequately differentiated lymphocytes, known as lymphoblasts, which arise from the bone marrow and various lymphatic organs, including lymph nodes, lymph vessels, spleen, tonsils, and Peyer's patches (1). These immature cells are morphologically similar to large blast cells (2). Certainly, in the pathogenesis of ALL in felines, the feline leukemia virus (FeLV) prominently contributes, accounting for approximately two-thirds of the etiological factors, with the ailment typically manifesting in juvenile cats (3,4). Approximately 60% to 80% of cats with ALL are FeLV positive (4-6). Leukemia in FeLV-negative cats is rare, accounting for <15% of all hematopoietic neoplasms (7).

In the context of ALL, there is an observed swift clinical progression, and animals diagnosed with this condition exhibit limited responsiveness to therapeutic interventions. The diagnostic process involves the identification of lymphoblasts within the circulatory system and bone marrow

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(8). The clinical symptoms are related either to the lack of normal hematopoietic cells or to the infiltration of neoplastic cells into the organs (9). Hematological parameters may exhibit non-regenerative anemia, neutropenia, and thrombocytopenia in feline subjects afflicted with this ailment. Notably, FeLV carriage is frequently observed in such cases, which correlates with a less favorable prognosis. (8). Although treatment response rates are low, CHOP-based chemotherapy regimens, which consist of cyclophosphamide, doxorubicin, vincristine, and prednisolone, remain a viable therapeutic approach. Furthermore, therapeutic data encompassing analgesic agents, immunostimulants, antimicrobial medications, and blood transfusion, are administered in accordance with the animal's clinical treatment regimen (3,8,10).

FeLV is an enveloped RNA virus found in the Gammaretrovirus genus of the family Retroviridae, which can increase the risk of developing certain types of cancer, including suppression of the immune system, anemia, and ALL in cats (11). FeLV is an exogenous agent that replicates in many tissues, including bone marrow, salivary glands, and respiratory epithelium. In the absence of an immune response following the first infection, the FeLV virus can extend its presence to the bone marrow and affect hematopoietic precursor cells (11). Certainly, it is observed that in cats with FeLV, the most frequently occurring form of leukemia is ALL (6). Although exact data on the frequency of leukemia and lymphoma are not readily available, it is observed that these forms of tumors are extremely rare in medical contexts.

This case report aims to report a case of a domestic cat with feline leukemia virus infection, diagnosed with acute lymphoblastic leukemia and followed up.

2. Case History

The study material was composed of a 2.5-year-old, brown, female, neutered, leukemia-vaccinated (twice) domestic cat brought to the Erciyes University Faculty of Veterinary Medicine Department of Internal Medicine clinic with complaints of loss of appetite, lethargy, stomatitis, gingivitis, vomiting, and diarrhea.

During the clinical examination, it was determined that the rectal body temperature was 38.1°C, the pulse rate was 182 beats/min, and the respiration rate was 18 respirations/min. Additionally, manifestations such as enlargement of mandibular lymph nodes, swelling in the frontal region of the head, ulceration and gingivitis within the oral cavity, inflammation of the anal sacs, malodorous diarrhea, and recurrent vomiting were observed. On the initial day of presentation at the clinic, the hematological assessment revealed the inability to read white blood cell values using the hematology device (Table 1). This result was not considered to fall within the typical range of leukocyte levels analyzed by the device. The biochemical evaluation revealed hyperproteinemia, hypernatremia, and hyperkalemia, as well as elevated values of AST, GGT, and GLU (Table 2). Based on these data, a symptomatic treatment protocol was established (Table 3). During the course of treatment, repeated hematological laboratory measurements were conducted. (Table 1). During the initial phase of treatment, although no improvement was observed, the owner of the patient recorded a worsening in the patient's overall health condition. Subsequently, suspecting enlargement in the patient's mandibular and femoral lymph nodes, a fine-needle aspiration biopsy was performed on the patient's popliteal lymph node. Furthermore, on the same day, the patient tested for FIV/FeLV rapid diagnostic kit (Asan Easy Test® FIV Ab/FeLV Ag), revealing a positive result for FeLV.

Table 1. Hematological parameters.

Measurement	1. Day	5. Days	36. Days	70. Days	Reference Ranges*
WBC (10^9/L)	-	-	3.2 **L**	12.5	5.5 - 19.5
LYMPH (10^9/L)	-	-	1.1 **L**	2.6	1.5 - 7
MON (10^9/L)	-	-	0.5	0.9	0 - 0.9
NEUT (10^9/L)	-	-	1.5 **L**	16.1 **H**	2.5 – 12.5
LYMPH %	-	-	36.2 **H**	13.3	27 - 36
MON %	-	-	15 **H**	4.2	0 - 5
NEUT %	-	-	46	81.1 **H**	45 - 64
RBC (10^{12}/L)	8.35	7.57	5.93	10.09 **H**	5 - 10
HGB (g/dl)	14.6	12.4	9.9	13.6	9.8 - 15.4
PCV %	38.6	33.8	29.1 **L**	36.2	30 - 45
MCV (fL)	46.2	44.6	49	35.9 **L**	39 - 55
MCH (10^9/L)	17.5 **H**	16.3	16.7	13.5	13 - 17
MCHC (10^9/L)	37.8	36.6	34.1	37.6	30 - 38
RDW (10^9/L) **	37.7 **H**	34.9 **H**	52.6 **H**	38.7 **H**	13.2 – 17.5
PLT (10^9/L)	171 **L**	139 **L**	116 **L**	1068 **H**	300 - 800
MPV (fL)	5.7 **L**	7.3 **L**	8.1 **L**	11.4 **L**	12 - 18
EOS %	-	-	2.8	1.4	0 - 4

Table 2. Biochemical parameters.

Measurement	1. Day	5. Days	36. Days	56. Days	Reference Ranges*
ALP (U/L)	81 **H**	73 **H**	92 **H**	89 **H**	0 - 45
GPT-ALT (U/L)	60.08	43.9	85.8	3.9 **L**	25 - 97
GOT/AST (U/L)	63.9 **H**	21.6	37.3	21.7	7 - 38
GGT (U/L) **	15 **H**	24 **H**	8	9	0 - 10
BUN (mg/dL)	24.29	15.88 **L**	22.89	22.42	19 - 34
CRE (mg/dL)	2.1	2.32 **H**	35.26 **H**	1.85	0.9 - 2.2
GLU (g/dL)	138.97 **H**	124.94 **H**	144.09 **H**	160.91 **H**	60 - 120
T. PRO (g/dL)	9.5 **H**	8.73 **H**	8.84 **H**	-	6 - 7.9
Na (mEq/L)	241.7 **H**	-	185 **H**	-	146 - 156
K (mEq/L)	8.09 **H**	-	5.61	-	3.7 - 6.1
ALB (g/dL)	-	4.08 **H**	4.92 **H**	4.48 **H**	2.8 - 3.9
P (mg/dL)	-	6.4 **H**	7 **H**	7 **H**	3 - 6.1
Ca (mg/dL)	-	-	11.46	-	8.7 - 11.7
AMYL (U/L)	-	-	1173	-	550 - 1458
Mg (mg/dL)	-	-	3.01	-	1.7 - 2.6

Table 3. Treatment protocol (3,15).

Drugs		Drugs Dose	Application Frequency	Application Method	Usage Period
Drugs Used in Symptomatic Treatment	Asist® 900mg sachet containing powder, Bilim Pharmaceuticals)	2 ml	BID	PO	One week
	Sülfametoksazol-Trimetoprim (Bactrim® 200/40mg/5ml Sol., Deva)	2.5 ml	SID	PO	One week
	Feniramin hidrojen maleat (Avil® 15mg/5ml Syrup, Sandoz)	1 ml	BID	PO	One week
	Sodyum Klorür (Polifleks® % 0.9 Isotonic)	75 ml	SID	IV	During the treatment
	Dekstroz (Polifleks® %5 Dekstroz)	75 ml	SID	IV	During the treatment
Aggressive Chemotherapy Drugs	Methylprednisolone (Prednol® 16mg pill, Gensenta)	2/3 pill	SID	PO	Four weeks
	Vincristine (Vincristine -Koçak® 2mg/2ml Inj., Koçak Farma)	0.2 ml	Once a week	İV	Four weeks
	Siklofosfamid (Endoxan® 50mg pill, Zydus)	1.5 pill	Once a week	PO	Four weeks
Food and Drugs Used for Regulating Kidney Functions and Increasing Appetite	Hill's PRESCRIPTION DIET Urgent Care (a/d)	During the treatment			
	Hill's PRESCRIPTION DIET Kidney Care (k/d)				
	Furosemide (Diüril®, 10 mg Inj., Vetaş)	1 ml	SID	IM	Five days
Drugs Used for Immunostimulant Purposes	Interferon alfa-2a (Roferon-A® 3Mıu/0.5 ml Inj., Roche)	50 IU	SID	SC	Fifteen days
	Asiklovir (Asiviral® 200 mg pill, Terra)	½ pill	SID	PO	Fourteen days
Drugs Used with the Onset of Nervous Symptoms and Constipation	Vitamin B_1-B_6 (Nervit®, 100/10mg/ml Inj., Vetaş)	1 ml	SID	SC	Seven days
	Gabapentin (Neurontin® 300mg caps, Pfizer)	0.5 ml	BID	PO	Ten Days
	Laktuloz (Osmolak® 667mg/250ml Sol., Biofarma)	3 ml	BID	PO	Five days

In the abdominal ultrasound examination conducted, it was determined that there was splenic enlargement (1.33 cm) and enlargement in the popliteal lymph node (short axis: 0.79 cm, long axis: 1.47 cm) Additionally, it was determined that there was a notable increase in the dimensions of the right kidney relative to reference values, and a distinction could be made between the renal cortex and medulla. Furthermore, no occurrences of cysts or neoplasms were observed in the cortex of the right kidney; its echogenicity was within the normal range, and no anomalies were detected in the collecting system. In the left kidney, it was determined that the size was below the reference values (3.8-4.4 cm), the cortex and medulla could be differentiated, there was no pericapsular fluid, the cortex of the left kidney was hyperechoic, and there were no formations such as cysts or neoplasms, and no abnormal findings were observed in the collecting systems of the kidney (Figure 1).

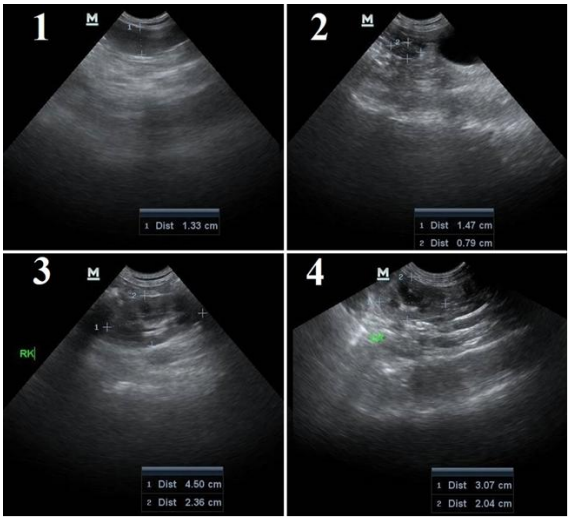

Figure 1. Ultrasonography (USG) images depict the following findings: Splenic enlargement and hypoechoic splenic parenchyma (1); enlargement of the popliteal lymph node (2); enlargement of the right kidney (3); reduction in size and increased echogenicity of the cortex in the left kidney (4)

In the microscopic examination of cytological preparations (Giemsa stain) (12) derived from the popliteal lymph node and peripheral blood smears, an excess of hyperchromatic medium and large-sized lymphocytes was observed, as evidenced by staining and scale measurements in the images. It was shown that the majority of neoplastic cells are made up of mononuclear cells, which belong to the lymphocyte class and exhibit marked atypia. The examined neoplastic cells were observed to have basophilic cytoplasm, varying in size of their nuclei. Some nuclei were intensely stained, while others appeared pale in color. In the examined preparations, pleomorphic cells and nuclear molding, considered indicative of malignancy, were identified. Nucleoli were predominantly situated towards the center of the nucleus and exhibited distinct characteristics (Figure 2, Figure 3, Figure 4).

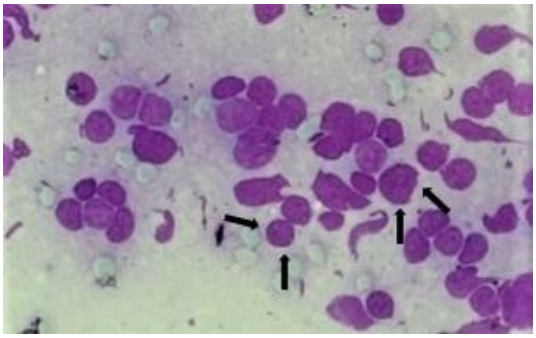

Figure 2. Hyperchromatic intermediate and large lymphocytes, variation in nuclear size (anisokaryosis) (Black arrows) among the cell nuclei. (Lymph node aspirate, giemsa strain, x400).

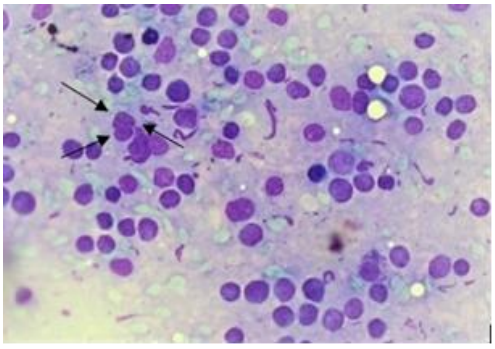

Figure 3. Nuclear molding (Black arrows). (Lymph node aspirate, giemsa strain, x400).

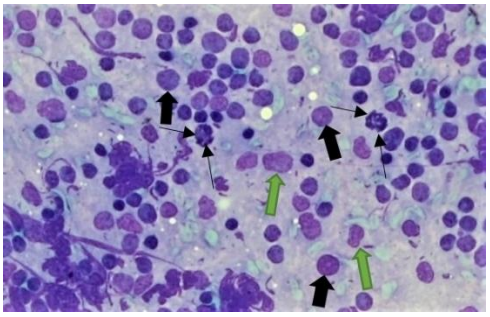

Figure 4. Abnormal mitosis (Thin arrows), Undifferentiated lymphoblasts (Thick arrows) at an incomplete stage of development, Pleomorphic cells (Green arrows). (Lymph node aspirate, giemsa strain, x400).

Based on the data, aggressive chemotherapy treatment spanning a period of four weeks was initiated for the patient diagnosed with ALL, as presented in Table 3. During the treatment process, repeated hematological assessments revealed the capacity of the hematology device to analyze leukogram data that had not been previously detected (Table 1). These analyses also identified manifestations of thrombocytopenia. In the second week of aggressive chemotherapy treatment, leukopenia and granulocytopenia

were observed, as shown in Table 1. Considering the values, prednisolone treatment was discontinued, and immunostimulant medication was initiated. Two weeks later, following the treatment course, blood samples were collected for hematological and biochemical laboratory analyses, as well as a blood smear. It was observed that the leukocyte count had increased (Table 1). Studies indicate that retrovirus infections may lead to kidney lesions (13-15). However, it should be noted that the normal toxicity of cytotoxic chemotherapeutic agents can be augmented in the presence of impaired liver and kidney functions. (3). During this period, in an effort to prevent renal damage in the patient, a renal diet regimen and diuretic treatment were recommended and prescribed to the owner of the patient, with the suggestion of monitoring the patient for a period of time. Two months later, during the follow-up examination, the patient was brought back to the clinic with an improved appetite but, at the same time, neurological symptoms characterized by incoordination in the hind limbs as well as constipation. Parenteral medication administration and enema were performed, and a laxative drug (lactulose) was prescribed. The treatment protocols administered are detailed in Table 3.

A few days following, it was observed that keratitis developed in the left eye, and a manifestation of lingual palsy occurred (Figure 5). Following the treatment protocols carried out for ten days after this date, although a general improvement in blood values was observed in the hematological assessment, there was no overall improvement in the patient's condition. Due to the persistence of neurological symptoms, a decision was made to initiate a different treatment protocol. For this purpose, the patient was administered pain management (16) and drugs to support neural stimulation (Table 3). This protocol was administered over ten days; however, due to the exacerbation of the patient's neurological symptoms (including incoordination in the forelimbs), the development of complete vision loss in the left eye (Figure 1), the persistence of constipation, and the emergence of neurogenic bladder, euthanasia was carried out at the request of the patient's owner.

Figure 5. The cat diagnosed with ALL and FeLV infection had tongue paralysis, complete blindness in the left eye due to severe keratoconjunctivitis, and visual loss that did not respond to treatment.

3. Discussion

ALL is a rare hematopoietic neoplasm encountered in both cats and dogs (17). This is the first case report of acute lymphoblastic leukemia in cats in Türkiye.

While it is more frequently reported in dogs compared to cats, the disease is predominantly observed in younger and middle-aged dogs, typically within the age range of 1 to 12 years (1,18). It has been reported that FeLV-positive cats, specifically, are more likely to get the disease at a relatively young age (typically under 4 years of age) (19). It has been reported that non-specific symptoms often related to the gastrointestinal system, such as lethargy, anorexia, vomiting, diarrhea, oral ulceration, gingivitis, and weight loss, manifest concomitantly with the acute onset of the disease (7,20). In our study, both the age range and the asymptomatic nature of these data are consistent with the case under consideration. Lymphoproliferative disorders are more commonly observed in companion animals than myeloproliferative disorders, and among domestic species, they are more prevalent in cats. Cats with lymphoproliferative disorders are commonly positive for FeLV, Feline Immunodeficiency Virus (FIV), or both (9). In our study, the rapid diagnostic test kit for FeLV yielded a positive result, while the FIV test showed a negative result. The exact role of FIV in ALL pathogenesis is still unknown at present (7). It is well-established that gammaretroviruses, which are the causative agents of FeLV, are more pathogenic than lentiviruses, the agents responsible for FIV, and are known to induce virus-associated neoplasms, primarily lymphoma, and leukemia (20,21). In FeLV-infected cats, hematological abnormalities such as normal hematological values, regenerative or non-regenerative anemia, neutropenia, lymphopenia, monocytopenia, and/or thrombocytopenia may be observed (11). In our case study, it was observed that in addition to mild mucosal pallor, there was no evidence of anemia in the hematological profile. However, alterations in hematological parameters were identified, including an increase in monocyte (%) values, as well as conditions such as lymphopenia, thrombocytopenia, and granulocytopenia. In the late stages of the disease, elevated RDW (Red Cell Distribution Width) (%) and reduced MCV (Mean Corpuscular Volume) (%) values garnered attention. Oliveira et al., in a FeLV-infected feline diagnosed with ALL, reported that thrombocyte abnormalities were not observed (10). In cats, the prevalence of lameness, ocular or neurological symptoms associated with myeloid leukemia is not as commonly observed as it is in dogs (7). Neurological symptoms such as keratitis, lingual palsy, and neurogenic bladder were observed in our study. In our case of feline acute lymphoblastic leukemia, the observation

of neurological manifestations has prompted the consideration of neurological symptoms in all cases of ALL in cats.

The assessment of cellular morphology conducted by Dobson et al. may assist in distinguishing between ALL and acute myeloid leukemia (AML) (3). In our case, the diagnosis of ALL was established by identifying an increase in the number of hyperchromatic intermediate and large-sized lymphocytes and alterations in cell morphology in peripheral blood smears and cytological preparations obtained from lymph nodes. Tomiyasu et al., examining patients with ALL, emphasized that a significant increase in the number of lymphoblastic cells in peripheral blood may not always be evident (17). Furthermore, it has been suggested that in the aspect of detecting lymphoblastic cells in peripheral blood, even if their quantity is limited, suspicion of this disease should be warranted.

Findings from serum biochemistry analysis are nonspecific and reflect underlying secondary disease processes in FeLV infection. The most prominent biochemical alterations in our patient include hyperproteinemia, hyperalbuminemia, hypernatremia, and hyperkalemia. While no significant difference was observed in terms of hyperproteinemia between non-infected cats and cats with progressive FeLV infection, it is notable that cats infected with FIV exhibit a higher likelihood of demonstrating hyperglobulinemia when compared to non-infected cats (11,22).

After the diagnosis was established for the case presented in the report, the patient survived for approximately 2.5 months. While the prognosis appears to be slightly more favorable compared to AML, approximately 20% to 40% of ALL cases achieve a state of remission. In general, there are typically short periods of survival lasting from one to three months; however, it has been noted that, on occasion, longer durations may be possible. It has been assessed that the course of the disease in our case is consistent with previous reports (3,11).

According to our case report, a FeLV-infected cat diagnosed with ALL has been reported for the first time in Türkiye. The current prevalence rate of FeLV in Türkiye is unknown. Feline leukemia, a viral infection, can give rise to various health issues in cats, including acute lymphoblastic leukemia. Cats infected with the FeLV are at risk of developing acute lymphoblastic leukemia, a type of cancer that affects white blood cells. Therefore, it is considered essential for veterinarians to be knowledgeable about the diagnosis, treatment protocols to be applied, the likely prognosis of the disease, and the implementation of preventive measures for FeLV-suspected or positive cats and hematopoietic neoplasms caused by this infection. Regular testing and vaccination against feline leukemia (FeLV) will aid in preventing the spread of the virus and reducing the risk of developing acute lymphoblastic leukemia in FeLV-infected cats.

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Conflict of interest: No conflict of interest has been declared.

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