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MICROBIOLOGY

Feline leukemia: a review

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ABSTRACT: Among the hematopoietic neoplasms, leukemias are caused by myeloid or lymphoid cells in the bone marrow, which can either be acute with an unfavorable prognosis and mostly affect cats that tested positive for feline viral leukemia (FeLV) or chronic in older cats that have a poor prognosis. Leukemias have several classifications in which the differentiation depends on complementary tests, such as blood profile, myelogram, cytology. and flow cytometry, which help determine the best treatment for the animal.
Key words: tumors, hematopoietic neoplasms, cat.

Leucemia felina: revisão

RESUMO: Dentre as neoplasias hematopoiéticas, as leucemias são originadas pelas células mieloides ou linfoides na medula óssea, podendo ser de forma aguda, com um pior prognóstico, principalmente, acometendo gatos com leucemia felina (FeLV positivos) ou, de forma crônica, que apresentam um prognostico reservado, especialmente em gatos idosos. As leucemias possuem várias classificações, cujas diferenciações irão depender de exames complementares como hemograma, mielograma, citologia e citometria de fluxo, importantes para a caracterização e para o melhor tratamento do animal.
Palavras-chave: tumores, neoplasias hematopoiéticas, gato.

INTRODUCTION

Hematopoietic tissue contains an average of one cell for every 500-1000 mature cells, with enormous amplification occurring during proliferation, differentiation, and maturation of blood cells. Pluripotent stem cells produce progenitor cells, whose development is restricted to one or two cell lineages after the precursor cells proliferate and mature to replace senescent peripheral blood cells (DALECK & DE NARDI, 2016).

Leukemia is a hematopoietic neoplasm originating from myeloid or lymphoid precursors in the bone marrow and can either be acute or chronic. The disease is rare in felines but occurs mainly in cats that are positive for feline immunodeficiency virus (FIV) and feline viral leukemia (FeLV) (CRISTO et al., 2020).

Chronic leukemias mostly occur in older cats and are considered rare. Conversely, acute leukemias occur more frequently, are much more severe, and affect a greater number of young FeLV-positive cats (PRIHIRUNKIT et al., 2008; CRISTO et al., 2020).

Treatment depends on the type of leukemia diagnosed, which is made through clinical findings, blood counts, myelograms, and advanced techniques such as flow cytometry. This uses the immunophenotyping method to characterize the cells involved, through markers and their fluorochromes (WORKMAN & VERNAU, 2003; CAMPBELL et al., 2013) (Table 1). The most relevant studies are shown in table 2.

Chronic leukemias

Chronic lymphocytic leukemia (CLL)

Chronic lymphocytic leukemia, also known as well-differentiated leukemia, is characterized by the presence of small, well-differentiated lymphocytes infiltrating the bone marrow, bloodstream, and other organs in some cases. They are morphologically indistinguishable from normal small lymphocytes; although, the marrow is usually infiltrated by mature lymphocytes (CAMPBELL et al., 2013).

The pathology is rare in feline medicine, and studies suggest that, when diagnosed, cats with CLL usually have 25,000-575,000 lymphocytes/µL of blood, accompanied by a myelogram showing

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Table 1 - Markers in immunophenotyping by flow cytometry in felines.

CD45	PAN LEUKOCYTE
CD34	MEDULAR PRECURSOR CELL (YOUNG CELL)
CD3	PAN LYMPHOCYTE
CD5	PAN LYMPHOCYTE
CD4	T HELPER LYMPHOCYTE
CD8	CYTOTOXIC T LYMPHOCYTE
CD79A	LYMPHOCYTE B
CD20	LYMPHOCYTE B
CD21+	LYMPHOCYTE B
CD11	MONOCYTES, MCROPHAGES, NK CELLS
MIELOPEROXIDASE	GRANULOCYTES, MONOCYTES
CD14	GRANULOCYTES, MONOCYTES, MACROPHAGES

an increase of more than 15-20% of nucleated cells being lymphocytes (WORKMAN & VERNAU, 2003; WEISS, 2005). The neoplastic lymphocytes are small to medium in size and are cited as being slightly larger than typical small lymphocytes (CAMPBELL et al., 2013).

Affected cats are usually older, with a mean age of 10-12 years, without racial predisposition and negative for FeLV. Half of the cats are asymptomatic at diagnosis, and the symptomatic ones may present with weight loss, lethargy, vomiting, diarrhea, hepatosplenomegaly, and lymphadenomegaly. In the blood count, anemia is reported in 50% of cases and thrombocytopenia in 11%, in addition to lymphocytosis (WORKMAN & VERNAU, 2003; CAMPBELL et al., 2013).

When making a diagnosis, clinical findings, blood counts, and myelograms must be associated with more advanced techniques, such as genetic rearrangement receptor (PAAR) PCR and immunophenotyping (CAMPBELL et al., 2013). The PAAR determines the clonal population of lymphocytes, although problems with reagents have been cited (AVERY & AVERY, 2007).

Immunophenotyping performs phenotypic characterization according to lymphocyte markers. Most cats with CLL show proliferation of T Helper lymphocytes and are positive for CD3, CD4, and CD5, and negative for CD8 on cytometry. A smaller percentage of cats have cytotoxic T proliferation (CD3+, CD5+, and CD8+); or a double negative T phenotype (CD3+, CD4-, CD8-, variable CD5) or B phenotype (CD21+) (CAMPBELL et al., 2013). In dogs, the T phenotype is known to lead to considerably longer survival than B (COMAZZI et al., 2011).

The differential diagnosis should include other causes of lymphocytosis in felines. Infectious diseases rarely cause the alteration, but there are reports of felines testing positive for FIV,

Table 2 - Some important studies on feline leukemia.

Author - Year	Major findings	Number of animals	Technique used
WORKMAN, H. C. & VERNAU, W. (2003)	Chronic lymphocytic leukemia in dogs and cats: the veterinary perspective	(n = 12)	Blood count, evaluations, and immunophenotyping
MOCHIZUKI, H. et al. (2012)	Use of PAAR in feline lymphoid neoplasms	(n = 57)	PCR analysis of *TCRγ* gene rearrangement
CAMPBELL, M. W. et al. (2013)	Complete description of chronic leukemia in cats	(n = 18)	Blood count, evaluations, and phenotypic (flow cytometry, immunohistochemistry) and/or PARR confirmation of a monomorphic or clonal lymphoid population
TOMIYASU, H. et al. (2018)	Characteristics of acute lymphoblastic leukemia	(n = 6)	Polymerase chain reaction for antigen receptor gene rearrangement, flow cytometry or immunohistochemistry

toxoplasmosis, *Cytauxzoon felis*, and cats infected with *Mycoplasma haemofelis*, with lymphocyte counts between 7,000-9,000/µL (AVERY & AVERY, 2007; CAMPBELL et al., 2013).

Hyperthyroidism in 7% of cases may cause lymphocytosis, the highest cited count being 9,000 lymphocytes/µL (THODAY & MOONEY, 1992). Hypoadrenocorticism and thymoma may also cause lymphocytosis in felines (AVERY & AVERY, 2007), while 5% of cats with lymphoma have lymphocytosis, with a count that can reach up to 80,000 cells/µL of blood (GABOR et al., 2000).

The disease in some studies is cited as indolent, and there are reports of stable cats without treatment for more than one year, despite the average being 1-6 months (WORKMAN & VERNAU, 2003; AVERY & AVERY, 2007). Therefore, treatment is only indicated for cats with clinical signs, significant cytopenia, peripheral involvement, or lymphocyte counts above 60,000/µL (WORKMAN & VERNAU, 2003).

The most cited treatment in the literature is the use of chlorambucil at a dose of 0.2 mg/kg, or 2mg/cat. every 2 days associated with prednisolone 1 mg/kg daily (CAMPBELL et al., 2013; DALECK & DE NARDI, 2016). Protocols based on cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) and cyclophosphamide, vincristine, and prednisolone (COP) are also cited, with the second obtaining a complete response in only 27% of cases (DALECK & DE NARDI, 2016).

The prognosis is considered poor to favorable, and when treatment based on chlorambucil and prednisolone is administered, response occurs in 88% of cases, with a survival rate of 1-2 years (WORKMAN & VERNAU, 2003; CAMPBELL et al., 2013).

Chronic myeloproliferative diseases

They are a group of pathologies in which the bone marrow produces excessively differentiated myeloid cells, resulting from a malignant expansion of multipotent hematopoietic stem cell (VALLI, 2002; DALECK & DE NARDI, 2016).

Chronic myeloid leukemia (CML)

Chronic myeloid leukemia, also known as chronic neutrophilic leukemia, is characterized by a clonal expansion of granulocytes in peripheral blood and bone marrow (VALLI, 2002), as this neoplastic proliferation of the neutrophilic series can occur concomitantly with that of eosinophils and basophils. The global leukocyte count is normally greater than 100,000 cells/µL, possibly including some immature cells, variations in size and shape, nuclear hypersegmentation, pyknosis, and nuclear fragmentation.

In humans, CML is characterized by the presence of reciprocal translocation between chromosomes 9 and 22: t (9; 22) (q34; q11.2), which produces the so-called Philadelphia chromosome (Ph), resulting in the creation of the BCR-ABL fusion gene (SOREL et al., 2017). Consequently, the diagnosis is based on findings of persistent neutrophilia with no other causes and the presence of the Philadelphia chromosome (LIESVELD & LICHTMAN, 2010).

CML is divided into three phases in human medicine: chronic, accelerated, and blastic. The clinical signs of the first are nonspecific, such as anorexia and weight loss, a hemogram with neutrophilia, eosinophilia, and basophilia, with anemia and thrombocytopenia being commonly observed (LIESVELD & LICHTMAN, 2010). Skin lesions and itching are common due to the high production of basophils and histamine. The blast phase is defined by the presence of more than 20% of blasts in peripheral blood or bone marrow, clusters of blasts in the marrow, or extramedullary disease, such as an accumulation of granulocytes in the liver and spleen (VARDIMAN et al., 2002).

CML is rarely reported in veterinary medicine, possibly due to the lack of characterization of the disease and the difficulty in making a diagnosis as there are few methods available to show the clonal proliferation of leukocytes. There are no genetic markers for CML in cats, and the disease can only be diagnosed after careful exclusion of other causes of leukocytosis, such as inflammation, infection, immune-mediated diseases, and other malignancies.

Clinical signs are varied, and many cats may be asymptomatic. The hematological changes that can be found are the same as those in humans, and cytometry can be used to complement the diagnosis. Complications such as hemorrhages and infections are cited, often evolving to the blast phase, and cats affected by the disease are often positive for FeLV (DALECK & DE NARDI, 2016).

In a 2014 report, an asymptomatic male cat had intense leukocytosis, with neutrophilia (62,000/µL), eosinophilia (7,700/µL), and basophilia (200/µL). Bone marrow aspirate confirmed the proliferation of myeloid lineage cells. The subject cat was followed up for 63 months without treatment. Seven months after diagnosis, it presented pruritus and skin lesions, in addition to an increase in serum histamine, similar to that cited in the human medical literature (MOCHIZUKI, 2014).

CML treatment is controversial as cats can live for long periods before a blast crisis is detected, and chemotherapy is unable prevent it. Supportive treatment consists of the use of a DNA synthesis inhibitor, known as hydroxyurea, at a dose of 25-50 mg/kg every 24 hours at induction, followed by maintenance treatment of 15 mg/kg every 24 hours, and then every three days when the values have been normalized (DALECK & DE NARDI, 2016).

Chronic eosinophilic leukemia (CLE)

Chronic eosinophilic leukemia is a variant of CML. High eosinophil counts above 15,000 cells/µL are observed and there may also be circulating young cells, in addition to eosinophilic infiltrates in peripheral organs. There is hyperplasia of eosinophilic precursors in the bone marrow and an increase in the myeloid/erythroid ratio (DALECK & DE NARDI, 2016).

A differential diagnosis should consider that eosinophilia is a common finding in cats, occurring in immune-mediated diseases, endo and ectoparasitism, infectious diseases, mast cell tumors, and hypersensitivity reactions, such as those that occur with the clinical presentation of eosinophilic dermatoses (GELAIN et al., 2006). In contrast, paraneoplastic hypereosinophilia and hypereosinophilic syndrome are uncommon. The second is characterized by peripheral and tissue eosinophilia, in addition to organ dysfunction, and can be classified as idiopathic, neoplastic, and paraneoplastic (BARRS et al., 2002).

Paraneoplastic hypereosinophilia (PH) and paraneoplastic hypereosinophilic syndrome (PHS) are usually associated with intestinal T-cell lymphomas, with the differentiation between these and LEC being the presence of the neoplasm, which must always have been diagnosed by histopathology. associated with immunohistochemistry (BARRS et al., 2002).

Their occurrence is most likely due to the secretion of interleukin 5 by neoplastic lymphocytes, which stimulate the production of eosinophils (BARRS et al., 2002). In cases of intestinal lymphoma, there are reports of hypereosinophilia, one with HPS with a count of 2,800 eosinophils/µL of blood (BARRS et al., 2002), and two with HP with a count between 21,000 (BALAN et al., 2017) and 96,000. eosinophils/µL of blood.

The clinical signs of CLE are variable. In one report, a three-year-old FeLV-positive feline presented with lethargy, weight loss, severe non-regenerative anemia, thrombocytopenia, jaundice, and dehydration. The eosinophil count was greater than 120,000//µL of blood, with some hypersegmented cells and dysplastic features. In bone marrow aspirate, 80% of the cells were segmented eosinophils, and liver, spleen, and mesenteric lymph nodes also had eosinophilic infiltrates (GELAIN et al., 2006).

Immunocytochemistry is invaluable when making the diagnosis and taken together with the blood count and the myelogram. In cases of CLE, the granulocytes are negative for myeloperoxidase, chloroacetate, and naphthyl acetate esterase; and positive for alkaline phosphatase. Monoclonal antibodies to antigens can be tested in flow cytometry, such as CD18 (all leukocytes), CD45-like (all leukocytes), CD3 (T lymphocytes), CD4 (T helper lymphocyte), CD8 (cytotoxic T lymphocyte), CD21 (B lymphocyte), CD11b (myelomonocytes), and CD14-PE (monocytes and macrophages) (GELAIN et al., 2006).

In a report by GELAIN et al. (2006), all leukocytes were positive for CD18 and CD45-like, 90% for CD11b, and 69% for CD14 in peripheral blood and bone marrow. The CD14 was also detected in PCR, and no previous study observed its positivity for feline eosinophils, even under physiological conditions. In contrast, CD11b positivity was expected as it is commonly positive for eosinophils and monocytes (GELAIN et al., 2006).

Hydroxyurea-based treatment of ECF can be applied, but cats respond poorly to it, suggesting the use of prednisolone 2mg/kg every 8 hours (DALECK & DE NARDI, 2016).

Chronic basophilic leukemia (CBL)

Although very rare, CBL has been reported in FeLV-positive cats, characterized by leukocytosis with high proportions of basophils in peripheral blood and bone marrow. Anemia, thrombocytosis, lymph node enlargement, and hepatosplenomegaly are cited as clinical signs (DALECK & DE NARDI, 2016).

Differential diagnoses should consider hypersensitivity reactions, inflammation, heartworms, and paraneoplastic syndromes associated with systemic mastocytosis (MEARS et al., 1997; BALAN et al., 2017). The basophil can be confused with the mast cell, given that both have toluidine blue positive cytoplasmic granules. To differentiate between the two in cytochemistry, tests can be performed for myeloperoxidase and vimentin (mark basophils), and C-kit and tryptase (mark mast cells). In flow cytometry, the basophil is negative for markers such as CD3, BLA36, CD136, and CD204 (MEARS et al., 1997).

Although rare, paraneoplastic basophilia has already been reported in cases of felines with intestinal lymphoma, the most intense type with basophil counts reaching 4,000 cells/µL of blood,

accompanied by eosinophilia and lymph node infiltration (BALAN et al., 2017).

A report of AML in a dog found 43,000 peripheral basophils, and 36% of the cells in the bone marrow were of the basophilic lineage; The dog itself had nonspecific clinical signs. The treatment consisted of the use of hydroxyurea, and the animal remained in remission for 21 months (MEARS et al., 1997).

When treating chronic basophilic leukemia, the doses of hydroxyurea used can be administered every 8 hours as neoplastic basophils are very sensitive to this substance. However, hydroxyurea may also lead to bone marrow suppression.

Polycythemia vera (PV)

PV, caused by primary (or idiopathic) polycythemia, manifests as an overproduction of normal red blood cells in the bone marrow, with the cloning of erythrocytes occurring even at normal or low levels of erythropoietin (EPO) (BEALE, 2017). It is considered rare and more often occurs in middle-aged cats (DALECK & DE NARDI, 2016).

Some theories suggest that this condition is due to hypersensitivity to EPO rather than a population of malignant cells in the marrow. Erythropoietin measurement has limited diagnostic value, perhaps because of this theory, but mainly owing to the lack of feline-specific tests.

Secondary polycythemia can occur due to heart disease, chronic lung diseases, renal cysts, or erythropoietin-producing renal neoplasms. Therefore, at the time of diagnosis, imaging tests, such as abdominal ultrasound, chest radiography and echodopplercardiogram, are essential (FENNEL, 2018).

The primary clinical signs are hyperstained mucous membranes, ears and pads, and splenomegaly. However, the disease is usually diagnosed only after the clinical signs have become severe. Blood hyperviscosity could lead to cerebral hypoperfusion, resulting in ischemic strokes that can lead to blindness, vestibular ataxia, and epileptic seizures, depending on the neuroanatomical region involved. As blood flow obstruction can occur due to vascular effects, secondary symptoms such as uveitis may be the first to be noticed.

The diagnosis of PV is considered simple, being confirmed by erythrocytosis associated with normal oxygen blood pressure and normal or reduced EPO concentration. Cases with very high hematocrits have been cited, in addition to the common occurrence of increased hemoglobin, leukocytosis, and thrombocytosis. Circulating erythrocytes are normal, and there is bone marrow hyperplasia, but with a normal myeloid/erythroid ratio (DALECK & DE NARDI, 2016).

Initial treatment aims to reduce the number of circulating erythrocytes through phlebotomy to stabilize the patient, with the volume being replaced through intravenous fluid therapy. Afterward, the patient can be managed at home with drugs and intensive follow-up with periodic blood counts (FENNEL, 2018).

Drug treatment consists of the application of hydroxyurea 125mg every 48 hours for two weeks. Afterward, maintenance occurs at a dose of 250mg, twice a week. Side effects of long-term use of hydroxyurea are generally reversible and include bone marrow suppression, hair loss, vomiting, and diarrhea.

The prognosis is favorable, and the therapy has a good response rate, despite the disease being cited as incurable. In cases of patients with severe adverse drug reactions, alternative treatment methods include periodic phlebotomies and other chemotherapeutic agents.

Acute leukemias

Acute lymphoblastic leukemia (ALL)

Acute lymphoblastic leukemia is a rare hematopoietic neoplasm in which young lymphocytes (or lymphoblasts) proliferate clonally in the bone marrow, being found in high concentrations in peripheral blood and marrow and occasionally in other organs. Furthermore, normal hematopoietic cells are often replaced by neoplastic cells in the bone marrow (TOMIYASU et al., 2018).

Among cats with ALL, 60-80% are positive for the feline leukemia virus (FeLV). This fact justifies the average age of cats affected by the disease, which is 5.5 years (TOMIYASU et al., 2018). It is also noteworthy that the most commonly diagnosed neoplasm in FeLV positive cats is lymphoma, and 25% of cats with lymphoma develop leukemic blood, with the lymphoblastic being the most frequent variety (DALECK & DE NARDI, 2016).

Commonly observed clinical signs are lethargy, anorexia, weight loss, fever, weakness, vomiting, diarrhea, hepatomegaly, and lymphadenopathy (DALECK & DE NARDI, 2016; TOMIYASU et al., 2018). In the blood count, anemia and thrombocytopenia are reported in most cases (TOMIYASU et al., 2018).

The criteria for diagnosing ALL in cats are the same as those for dogs, and consist of: (1) more than 20% of the nucleated cells in peripheral blood are blasts or 30% in the bone marrow, which is usually hypercellular, with intense lymphoblast infiltration and variable number of pro-lymphocytes (DALECK

& DE NARDI, 2016); (2) blasts confirmed to be of lymphoid origin; anemia, neutropenia, or concomitant thrombocytopenia (BENNET et al., 2017).

An increase in the number of circulating lymphoblasts is commonly observed, though not in all cases. In one study, blasts above 10,000/µL of blood were found in 66% of cats, and more than 30% among nucleated cells in 83.3%. Furthermore, the number of blasts in the peripheral circulation is not proportional to the bone marrow (TOMIYASU et al., 2018). Of the cats with subleukemic leukemia, one had only 1770 leukocytes/µL of blood, with 530 blasts (30% of blasts in peripheral blood) (TOMIYASU et al., 2018).

In some cases, it may be impossible to differentiate lymphoid blasts (Figure 1) from myeloid blasts through morphology alone, and other diagnostic tools may be necessary (AVERY & AVERY, 2007). The lymphoid origin of the blasts must always be confirmed by PAAR, flow cytometry, or immunohistochemistry (MOCHIZUKI et al., 2011; MOCHIZUKI et al., 2012). Despite the T immunophenotype being cited as the most common (DALECK & DE NARDI, 2016), in a study with six cats, four had immunophenotype B, one T, and another had an undetermined phenotype, confirmed by flow cytometry or immunohistochemistry. The PAAR was false negative in three cases (TOMIYASU et al., 2018), a higher rate than that found in previous studies (MOCHIZUKI et al., 2011; MOCHIZUKI et al., 2012)

Treatment consists of chemotherapeutic protocols, such as COP (COTTER, 1983), CHOP (TOMIYASU et al., 2018), and LOPH (HORTA et al., 2021). In one study, cats treated with COP had a median survival of seven months (COTTER, 1983). However, in a recent study with CHOP or L-asparaginase or prednisolone, survival ranged from 1 to 115 days, with a median of 55 days. The cat treated solely with prednisolone survived for 33 days (TOMIYASU et al., 2018).

The prognosis of ALL is unfavorable, being considered a fatal disease with an average survival of less than two months (AVERY & AVERY, 2007). Early diagnosis is important, and it should be remembered that the number of circulating blasts is highly variable. Therefore, any case of circulating lymphoblasts should be carefully studied (TOMIYASU et al., 2018).

Acute myeloid leukemia (AML)

Acute myeloid leukemia is a neoplastic disease of the bone marrow associated with clonal disorders of hematopoietic stem cells, considered rare in feline medicine (TAGAWA et al., 2020), but

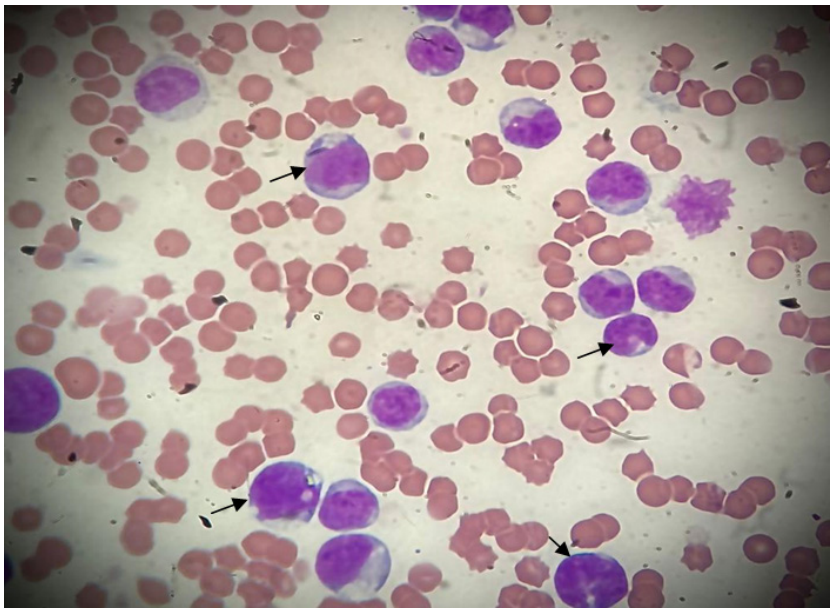

Figure 1 - Peripheral blood smear from a feline with acute myeloid leukemia. High concentration of blast cells, morphologically indistinguishable from blast cells of lymphoid lineage (black arrows). Giemsa stain, 40x. (Personal archive).

when it occurs, it is more frequent in cats that test positive for FeLV or FIV (MYLONAKIS et al., 2008; CRISTO et al., 2019).

In a study of 37 cats diagnosed with leukemia, most of them were young and FeLV positive, and 56.8% had AML (CRISTO et al., 2019). This fact is most likely due to the chromosomal translocation induced by the retrovirus, involving chromosome 11q23, and the rearrangement of a leukemia gene (myeloid, lymphoid or mixed lineage) at the translocation interruption point (PRIHIRUNKIT et al., 2008).

Leukocytosis is marked in most cases of AML, and some cats have leukocyte counts above 100,000/µL of blood, in addition to circulating blasts representing more than 20% of nucleated cells, making the differentiation between myeloid and lymphoid blasts especially challenging (CRISTO et al., 2019). The myelogram shows an increase in immature forms and hypoplasia in the other series (TASCA et al., 2009). Blast infiltration in lymph nodes, spleen, and liver may also occur (MYLONAKIS et al., 2008).

AML is classified into subtypes, according to the origin and degree of differentiation of blast cells: undifferentiated M0, M1 myeloblastic with minimal maturation, myeloblastic M2 with maturation, promyelocytic M3, myelomonocytic M4, M5 monocytic, M6 erythroleukemia, and megakaryoblastic. The AML M1, M2, and M6 are the most common in felines (TAGAWA et al., 2020).

Differentiating between subtypes can be very difficult through cell morphology or peripheral blood and bone marrow smear evaluations as inconclusive results are common (MYLONAKIS et al., 2008). Furthermore, AML can often be confused with ALL if only these methods are used to study the cells. The evaluation of the cell by transmission ultrastructure (TEM) or a scanning electron microscope (SEM) can help provide a more accurate reading (PRIHIRUNKIT et al., 2008).

As a rule, the differential diagnosis is made by the presence of azurophilic granules and Auer rods in cells of myelocytic origin and their absence in cells of lymphocytic origin. However, cytochemical investigation and immunophenotyping are also indicated when making a diagnosis (PRIHIRUNKIT et al., 2008; DALECK & DE NARDI, 2016).

Another important differential diagnosis refers to leukemoid reactions associated with infections and inflammation. Evidence of inflammation and changes suggestive of infections in WBC should always be checked and tests should be performed for infectious diseases, such as mycoplasmosis and ehrlichiosis (PRIHIRUNKIT et al., 2008; MYLONAKIS et al., 2008).

Clinical signs are nonspecific, such as apathy, anorexia, weight loss, fever, hepatosplenomegaly, and lymph node enlargement. In addition, anemias, neutropenia, and thrombocytopenia are common, and coagulopathies are important complications in cats with AML (TAGAWA et al., 2020). In a study of 33 dogs, 97% had anemia, while 88% had thrombocytopenia (TASCA et al., 2009).

In one case of a FeLV-positive feline with myelomonocytic leukemia (M4), 54,400 leukocytes/µL were found, with 29% blast cells (30% nucleated cells). Most cells expressed lysozyme, indicating monocytic lineage (MYLONAKIS et al., 2008).

Monocytic leukemia (M5) represents less than 5% of leukemias diagnosed in cats, and in a 2020 report, a 12-year-old feline with weight loss, anorexia, and tachypnea was diagnosed. The blood count found 137,000 leukocytes/µL of blood, 73% of which were monocyte blasts, along with anemia and thrombocytopenia. Treatment with doxorubicin and cytosine arabinoside proved to be effective, but without any improvement in the anemia and thrombocytopenia, highlighting the importance of blood transfusion in patients with AML (TAGAWA et al., 2020).

Treatment can be performed with several chemotherapy protocols, but success rates are very low. The use of agents such as doxorubicin, cytosine arabinoside, cyclophosphamide, prednisolone, and vincristine have already been used in the form of mono and polychemotherapy, both without success. Other protocols, such as CHOP, COP and LOPH, the same used for ALL, have been mentioned (DALECK & DE NARDI, 2016; TAGAWA et al., 2020; HORTA et al., 2021).

A prognosis of AML is unfavorable, with a median survival rate of three to eight weeks (DALECK & DE NARDI, 2016; TAGAWA et al., 2020). The disease progresses very quickly, leading to important cytopenias in peripheral blood and bone marrow suppression by neoplastic cells (MYLONAKIS et al., 2008).

CONCLUSION

Despite not being the most common type of hematopoietic neoplasm, feline leukemias are frequently diagnosed in feline medicine, especially in young, FeLV-positive cats. Acute leukemias (AL) are more commonly reported, with the lymphoid lineage being the most cited, despite the fact that, in a recent Brazilian study, myeloid cells prevailed. ALs are very serious diseases with poor response to treatment and poor prognosis. The diagnosis of leukemias must be associated with clinical alterations, blood counts,

myelograms, and more complex tests, such as flow cytometry, PAAR, and immunocytochemistry, if necessary. Treatment varies depending on the disease in question, as well as the prognosis.

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DECLARATION OF CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

AUTHORS' CONTRIBUTIONS

The authors contributed equally to the manuscript.

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