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CASE REPORT
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Myelodysplastic Syndrome Progression to Acute Myeloid Leukemia in a Cat FeLV Seroreactive

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ABSTRACT

Background*:** Acute myeloid leukemia (AML) is a group of non-lymphoid hematological tumors characterized by aberrant proliferation and/or decreased apoptosis of a clone of non-mature cells, resulting in the accumulation of immature blast cells in the bone marrow and peripheral blood. It is considered rare, as it represents 10% of neoplasms of hematopoietic origin. However, it is known that felines seroreactive for FIV and FeLV are more predisposed and reports of this type of leukemia in cats in the literature are scarce. Thus, the objective of this study was to evaluate the blood and bone marrow of a cat seroreactive for FeLV that presented with myelodysplastic syndrome that progressed to acute myeloid leukemia. ***Case: A 6-year-old male mixed-breed cat, neutered, seroreactive for FeLV, showed apathy, weight loss, and pale mucous membranes. Initial peripheral blood smear evaluation revealed hypochromic normocytic anemia, leukopenia, neutropenia, lymphopenia, and thrombocytosis with many macropackets and giant platelets. Based on this blood picture, a long-spectrum antimicrobial therapy with amoxicillin and clavulanate [Clavulin® BD - 25 mg/kg, every 12 h] was started. Granulocyte colony stimulating factor used filgrastim (rHu G-CSF) [Fiprina® - 5 µg/kg, SC, every 48 h] and appetite stimulant mirtazapine [Mirtz® - 2 mg/cat, orally, every 48 h] were used to correct leukopenia and nutritional status, respectively. Follow-up blood smear evaluation on the 30th day showed persistence of the hematological changes noticed earlier. A bone marrow puncture was performed, and immunosuppressive therapy with prednisolone [Predsim® - 4 mg/kg, orally, every 24 h] was initiated. The aspirated material showed increased cellularity for age, decreased myeloid:erythroid ratio, and 39.8% of blasts of myeloid origin. An average of 17.7 megakaryocytes were observed per field (10x magnification). Bone marrow cytological evaluation suggested acute myeloid leukemia with dysmegakaryocytopoiesis. After the diagnosis, the examinations were repeated monthly, and there was still intense leukopenia. However, in view of the stable clinical status and leukopenia with neutropenia, treatment for leukemia was not instituted and only supportive treatment was administered when necessary. Eight months after the diagnosis, clinical status had worsened, and unlike the earlier hemograms, global leukocyte count had increased with predominant lymphocytosis (95% of the total leukocytes) with atypical lymphocytes. The cat died a few days later.
Discussion: Bone marrow evaluation is indicated when peripheral blood cell abnormalities are present and cannot be explained in the context of the clinical history. In the present report, the bone marrow aspirate was hypercellular (cellularity above 75%); however, intense leukopenia was observed in the peripheral blood. In myelodysplastic syndromes, it is common for the bone marrow to be normal to hypercellular, which occurs when there is a greater production of myeloid or erythroid cell lines in response to the loss, destruction, or consumption of cells. Despite this, cytopenias may be present in the peripheral blood, since the defective cells undergo apoptosis and die before being released into the circulation, characterizing inefficient hematopoiesis. The diagnosis of acute leukemia comprises a variety of hematopoietic neoplasms that are complex and unique. Each acute leukemia subtype has defining characteristics that affect the prognosis and treatment of each animal.

Keywords: tumours, myeloid neoplasm, SMD, LMA, bone marrow cytology, feline.

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INTRODUCTION

Myeloproliferative disorders are subclassified as Myelodysplastic Syndrome (SMD), Acute Myeloid Leukemia (LMA), and myeloproliferative neoplasms (NMPs). Hematopoietic neoplasms can be broadly classified as lymphoproliferative and myeloproliferative based on morphological features. In acute myeloid leukemias, there is a dominance of immature myeloid precursors (blasts) in the bone marrow. They are also classified as acute or chronic, based on the degree of cellular differentiation [22,23]. These tumors are rare because they represent 10% of neoplasms of hematopoietic origin, but occur more frequently in cats due to an association with the feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) [8,24].

It is of great importance to evaluate the marrow when there is a suspicion of some hematological abnormality, which is indicated when the blood smear is not able to give answers about what is causing such abnormality, such as cytopenia in one or more cell lines. Thus, among the evaluation techniques, the bone marrow aspirate, because it is easy to perform, cheap, provides rapid diagnostic information, is the most chosen for bone marrow evaluation [9,10,17].

In veterinary medicine, despite the LMA being considered the most common presentation, there are still few reports of this type of leukemia in domestic cats [1,2,21]. Thus, the objective of this work was to describe the evaluation of the blood and bone marrow of a seroreactive feline for FeLV who had Myelodysplastic Syndrome, which progressed to Acute Myeloid Leukemia.

CASE

Feline, mixed breed, male, six years old, neutered, positive for the virus FeLV, presented a picture of apathy, weight loss, and pale mucous membranes, leading to the initial suspicion of mycoplasmosis.

Initially, the patient's blood count was requested, being performed through the hematological counter pocH-100iv (Sysmex®)[1], specific leukocyte counts and cytomorphological evaluations were performed by the manual method of microscopic evaluation, and the findings were: hematocrit 23.2% (27,0 - 45.0%), global leukometry 2.000/µL (5.500 - 19.500/ µL), segmented 840/µL (2.500 - 12.500/µL), lymphocytes.160/µL (1.500 - 7.000/µL), platelet count 900.000 cel/µL (300.000 - 700.000 cel/µL) thus characterizing hypochromic normocytic anemia, leukopenia, neutropenia, lymphopenia, and thrombocytosis [19]. During the morphological evaluation of the platelets, many macropackets and giant platelets were evidenced, as shown in Figure 1.

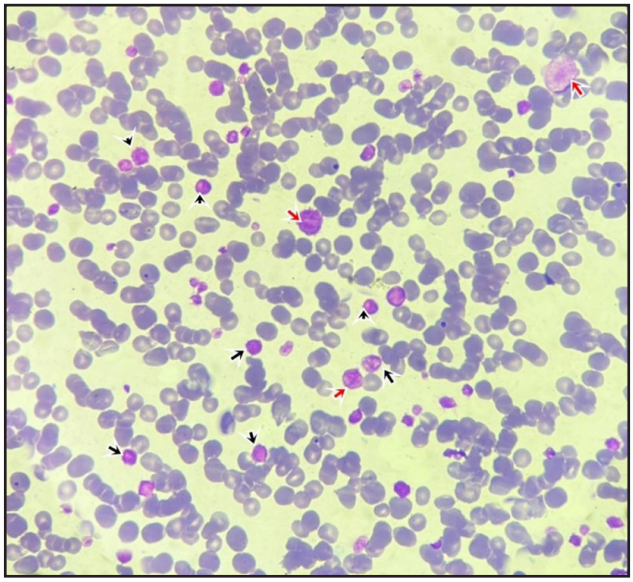

Figure 1. Photomicrograph of the hematologic extent demonstrating the presence of macroplatelets (black arrows) and giant platelets (red arrows). [Wright-Giemsa; 1000x].

The treatment initially instituted was an attempt to prevent the development of bacterial translocation sepsis with long-spectrum antibiotic therapy with amoxicillin with clavulanate[2] [Clavulin® BD - 25 mg/kg, every 12 h]. For the correction of leukopenia and neutropenia, a granulocyte colony-stimulating factor was used filgrastim (rHu G-CSF)[3] [Fiprina® - 5 µg/kg, SC, every 48 h]; mirtazapine[4] appetite stimulant [Mirtz® - 2 mg/cat, VO, every 48 h].

Thirty days after the start, a new blood count was requested and the hematological changes persisted. Bone marrow puncture was performed in the proximal humerus epiphysis region and immunosuppressive therapy with prednisolone[5] [Predsim® - 4 mg/kg, VO, every 24 h] was started.

The aspirated material showed occasional bone spicules with increased cellularity for age (above 75% of cells) and a decreased myeloid: erythroid ratio of 0.54. An average of 17.7 megakaryocytes were observed per field with a 10x magnification, representing an increase in the megakaryocytic series, composed predominantly of dwarf megakaryocytes and immature megakaryocytes exhibiting dysplastic alterations (Figure 2).

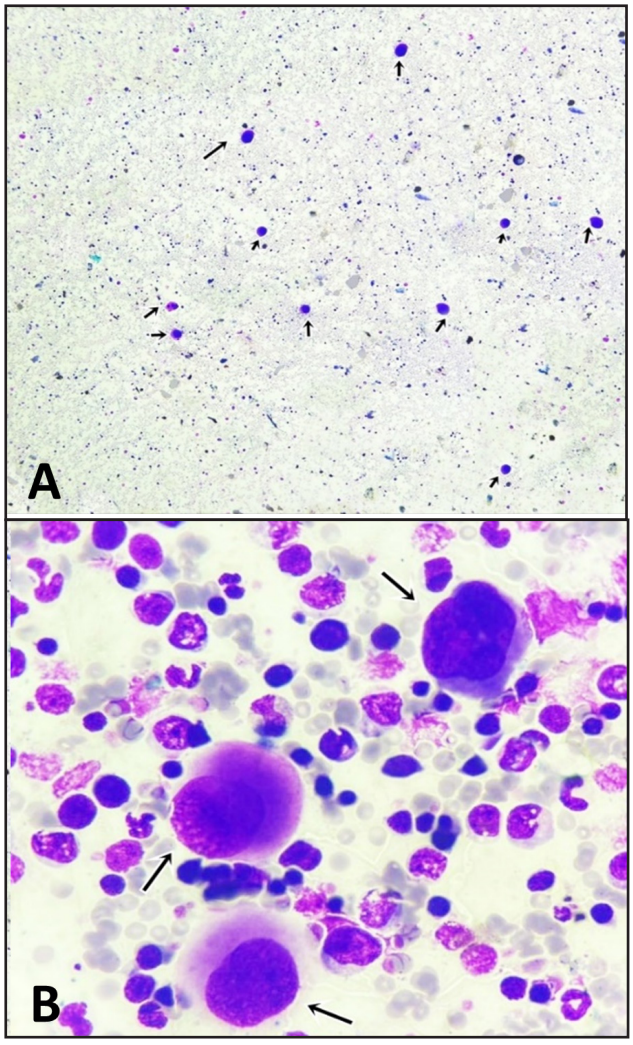

Figure 2. A- Photomicrograph of bone marrow aspirate showing megakaryocytes [100x]. B- Photomicrograph showing immature megakaryocytes [1000x]. [Wright-Giemsa].

The granulocytic series was reduced, with disordered maturation, with the maintenance of the percentage of immature elements and decrease of mature elements, being composed predominantly by rod and segmented neutrophils. The erythroid series showed disordered maturation, with an increase in immature elements. In the lymphocytic, plasmacytoid and monocytic series were normal to decrease 39.8% of blasts of myeloid origin were observed (Figure 3). No microorganisms or neoplastic cells were observed, and no increases in iron/hemosiderin stores were observed. Cytological evaluation of the bone marrow suggested acute myeloid leukemia and dysmegakaryocytopoiesis.

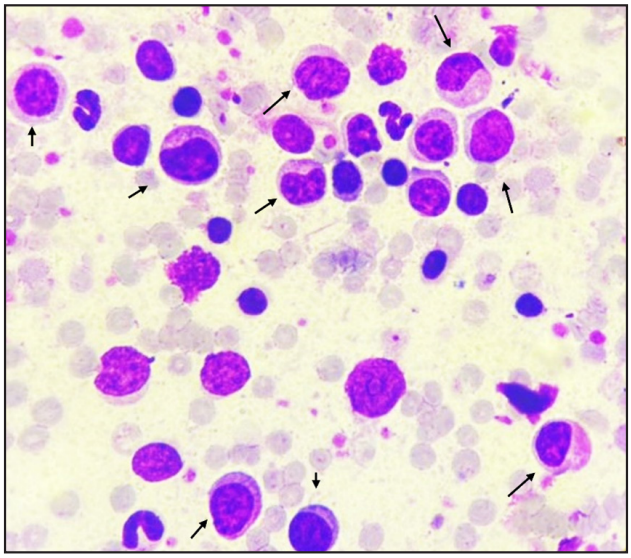

Figure 3. Photomicrograph of bone marrow aspirate showing myeloid precursors. [Wright-Giemsa; 1000x].

After the diagnosis, the exams were repeated monthly, and there was still intense leukopenia. Due to the feline's stable clinical status and leukopenia with neutropenia, the treatment for leukemia was not instituted, with only supportive treatment being given when necessary.

Eight months after the start of supportive treatment, the patient's clinical status worsened, with anorexia and weight loss. The blood count performed showed an increase in leukocytes concerning previous tests with a global leukocyte count of 15.900/µL and lymphocytosis of 15.105/µL with atypical lymphocytes, these being 95% of the total leukocytes. The animal died a few days later. The necropsy was carried out, and only the spleen was enlarged, with no macroscopic changes in the other organs.

DISCUSSION

Bone marrow evaluation is designated when peripheral blood cell abnormalities are present and cannot be related to the context of the clinical history, physical examination, or other additional diagnoses such as diagnostic imaging [8,20,28]. In the present report, the hematological findings could not be explained by the clinical picture of the animal, which is why the myelogram was performed.

In the present report, the bone marrow aspirate of the animal showed increased cellularity for age (above 75%), even so, intense leukopenia was observed

in the peripheral blood. According to Raza *et al*. [18], in myelodysplastic syndromes, it is common for the bone marrow to be normal to hypercellular. This increase in cellularity occurs when there is greater production of myeloid or erythroid cell lines in response to the loss, destruction, or consumption of cells. Despite this, it may present cytopenias in the peripheral blood, since the defective cells undergo apoptosis and die before being released into the circulation, characterizing inefficient hematopoiesis [13].

The maturation and morphology of the erythroid and granulocytic series should be evaluated to determine if it is complete and ordered, and thus to verify if an abnormality is present [14]. In the evaluation of the erythroid series of the present case, disordered maturation was found, with an increase in immature elements, and the granulocytic series was decreased, with also disordered maturation. According to Hoff *et al*. [13], the reason M/E decreased is indicative of increased erythroid production (erythroid hyperplasia) and decreased neutrophil production (myeloid hypoplasia) or a combination of the two.

During the cytological evaluation of the bone marrow, an average of 17,7 megakaryocytes per 10x magnification field was observed with a predominance of dwarf and immature megakaryocytes exhibiting dysplastic alterations, thus representing an increase in the megakaryocytic series, thus justifying the intense thrombocytosis present. These findings, according to some authors [5,6,7] may also be indications that the LMA originated from SMD. Walter *et al*. [27] demonstrated that the most likely interpretation is that the acquisition of additional driver mutations leads to the formation of hematopoietic cell subclones with further impaired differentiation and/or maturation ability. The proportion of blast cells progressively increases over time and eventually develops LMA evident.

In the case described, no treatment was instituted, due to intense leukopenia, since most of the cytotoxic drugs used for treatment, such as vincristine, can cause significant myelosuppression in a cat. The patient also had neutropenia, which is one of the most common complications of chemotherapy and is the main dose-limiting factor. Low neutrophil counts can be life-threatening, with chances of sepsis in felines. Thus, only supportive treatment was performed when necessary [24].

The feline leukemia virus (FeLV) is a retrovirus with oncogenic potential, capable of infecting cells of the immune system that induce immunosuppression and predisposition to opportunistic diseases of an infectious-parasitic nature or to comorbidities such as the emergence of neoplasms or dysplastic changes in the bone marrow [3,15,16]. A previously study showed a close relationship between infection by FeLV and feline leukemias where the ratio of myeloid to lymphocytic leukemias was approximately 2 to 1, respectively [8]. FeLV- positive cats are 62 times more likely to develop lymphoid neoplasms, myelodysplastic syndromes, and leukemic conditions than uninfected cats [12]. Months after the diagnosis of LMA. In the last hemogram, the increase in leukocytes and the inversion of the proportion of neutrophils and lymphocytes were verified. Lymphocytes were atypical and represented 95% of total leukocytes. Besides having myeloid neoplasia, another concomitant disease, such as lymphoproliferative disorders in the leukemic phase, such as lymphoma or acute lymphoblastic leukemia (LLA) may have also installed itself, thus justifying the increase in leukocytes and lymphocytes [3,8,23].

At necropsy, the only macroscopic alteration observed was splenomegaly. This finding corroborates with the study carried out which found that 4 of the 7 cats with LMA (57,1%) had enlarged spleens (between 2 and 10 times the normal size) and according to Tarrant *et al*. [25,26], this would be due to infiltration by cells in the spleen.

The diagnosis of acute leukemia comprises a variety of hematopoietic neoplasms that are complex and unique. Each subtype of acute leukemia has specific characteristics that affect prognosis and treatment a recent study using an immunohistochemical marker showed promise in the diagnosis of acute myeloid leukemia used in cats [4,21]. The side effects of chemotherapy and its relative effectiveness make the search for a specific diagnosis the first goal in the management of leukemic patients [24].

The prognosis of LMA is often unfavorable and chemotherapy treatment often does not cause remission, so the disease is usually fatal [2].

It is concluded that due to the cytopenia of 2 lineages and dysplastic alterations in the cells as well as disordered maturation and increase in immature elements, it is suggested that the feline had a Myelodysplastic Syndrome, which would progress to Acute Myeloid Leukemia.

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***Declaration of interest*.** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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