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SECONDARY CARDIAC INVOLVEMENT OF MEDIASTINAL T-CELL LYMPHOMA IN A YOUNG SCOTTISH FOLD CAT - CASE REPORT

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Abstract

Mediastinal lymphoma in cats affects the lymph nodes in the cranial mediastinum and/or the thymus. The tumor comprises 10-20% of feline lymphomas. Males appear to be overrepresented. A 2-year-old neutered male Scottish Fold cat with hypertrophic cardiomyopathy treated according to the results of the medical investigation was presented for a second opinion consult. X-ray examination showed a gigantic neoplastic mediastinal mass, and the ultrasound examination revealed a right-sided deviation of the heart axis. Due to the poor prognosis, the cat was euthanized, and the necropsy was performed. Mediastinal T-cell lymphoma with neoplastic invasion into the pericardium and discreetly into the epicardium was diagnosed based on gross pathology, histopathology, and immunohistochemistry. The left atrium presented endocardial fibroelastosis, while the ventricular myocardium showed intercellular edema, myocardocyte laceration, vacuolar and hyaline degeneration, and necrosis in small, isolated areas. Additionally, the lung displayed diffuse collapse, edema, and congestion.

Key words: *fibroelastosis, T- lymphocytes, heart metastasis, CD3, immunohistochemistry.*

INTRODUCTION

Lymphoma (lymphosarcoma) is an aggressive malignant tumor of a group of lymphoreticular cells and often is originated in lymphoid tissues but may also occur in non-lymphoid organs (Shih, Brenn, & Schrope, 2014). The incidence is 0.2%, which accounts for 90% of all diagnosed neoplasms in cats (Burgess, 2020). It often grows as a solitaire tumor, but could be multicentric, non-visceral, or presents visceral involvement.

According to the literature, feline lymphoma is divided by anatomic classifications in mediastinal, leukemic, gastrointestinal, multicentric, and miscellaneous sites, like the kidneys, nasal, laryngeal or tracheal, central nervous system, and skin (Mori et al., 2019; Shih et al., 2014).

Clinical signs are associated with anatomical localization of the primary tumor and its metastases, including dyspnea, lethargy, anorexia, and emesis, or may not show clinical signs until the last stage. In cats, the location of the tumor is a determinant of clinical signs and prognostic (Burgess, 2020).

For feline lymphoma exists a bimodal age pattern distribution. In the young-age group, in addition to the lymph nodes, lymphoma can also affect the thymus in the cranial mediastinum (Alejandro et al., 2019; Sunpongsri et al., 2022). Retrovirus−positive cats present the neoplasm at a young age (1-3 years), and virus−negative cats present at an older age (10-13 years). The median age at tumor development is approximately of 11 years. There is no gender nor breed predilection, but Siamese and Siamese-related breed cats are overrepresented, suggesting a genetic susceptibility to the disease (Alejandro et al., 2019; Burgess, 2020; Seo et al., 2006). However, in some studies, the male had a greater ratio than the female, with a ratio 2.1: 1 (Sunpongsri et al., 2022).

Like in the presented case, mediastinal lymphoma is assumed to appear frequently in young cats (Burgess, 2020; Twomey & Compendium, 2005).

MATERIALS AND METHODS

A Scottish Fold neutered male cat, aged two years, weighing 3.6 kg, with hypertrophic cardiomyopathy treated according to the results of the medical investigation, was presented for a second opinion consult. In its medical records, the cat was diagnosed with hypertrophic cardiomyopathy class C and a small quantity of pleural effusion. Also, a month ago, the blood examination results revealed a high level of aspartataminotransferase, creatin kinase, triglycerides, calcium, and magnesium. The NT-proBNP was 50/pmol/L, and the lymphocytes were under the physiological level. Treatment with amlodipine, torasemide, and clopidogrel was prescribed. At the present consult, the gingival mucosa was pink, and the temperature was 38.6°C. Auscultation revealed diminished pulmonary and cardiac sounds.

Thoracic X-rays were performed with the patient in latero-lateral recumbency, and ultrasound with the patient in latero-lateral left and right recumbency.

Based on imagistic results, a gigantic intrathoracic mass, possibly originating in the thymus or mediastinal or sternal lymph nodes, was suspected. Due to the poor prognosis, the cat was euthanized, and the necropsy was performed.

The post-mortem examination was performed, and samples were collected for histopathological and immunohistochemical examination from all the modified organs. Cytological impression smears of the mediastinal mass were performed, air-dried, and stained with May Grunwald Giemsa (MGG) for light microscopy evaluation. The selected specimens from the free and involved organs were fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin wax, cut into 3 µm sections, and stained with hematoxylin and eosin (HE). For immunohistochemistry, primary antibodies for B-lymphocyte proliferation and differentiation PAX-5 (SP34) Rabbit Monoclonal Antibody were used, and to qualitatively identify T-lymphocytes, CONFIRM anti-CD3 (2GV6) Rabbit Monoclonal Primary Antibody were used. The samples were automatically processed using Ventana BenchMark ULTRA system.

RESULTS AND DISCUSSIONS

Cardio-respiratory diseases often require radiographic and echocardiographic examination for diagnostic approach. In this case, the chest x-ray examination of latero-lateral incidence revealed a severe, diffuse, increased radio-opacity of the cranial and cardiac thoracic region with soft tissue density, in 81 x 57 mm dimension, suggestive of a gigantic mediastinal mass (Figure 1*)*. The trachea was partial collapse in the middle and posterior third.

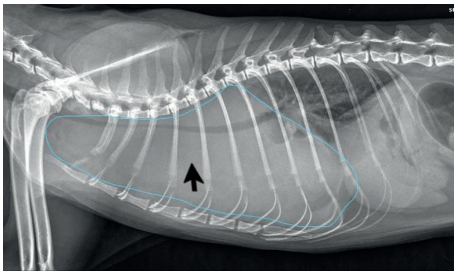

Figure 1. Right lateral thoracic radiograph depicting a large cranial and cardiac mediastinal mass (encircled), partial tracheal collapse (arrow), and lung displacement

Subsequently, cardiac ultrasound examination revealed a right-sided deviation of the heart axis, cardiac frequency of 120 beats per minute (BPM), and regular sinusal rhythm. In B-mode interventricular septum in diastole (IVDS) measured 3.0 mm, the left ventricular chamber diameter in diastole (LVDd) 15.0 mm, the left ventricular wall in diastole (LVWD) 3.0 mm, left ventricular chamber diameter in systole (LVDs) 8.0 mm and fractional shortening (FS) 46%. Blood pressure was 110 mmHg Doppler. All those measurements are consistent with no pathological findings.

The post-mortem examination revealed a large, smooth, tan, multinodular mass, extended into the mediastinum and enveloping the heart (Figure 2), involving the parietal surface of the pericardium. The mass also surrounded the proximal descending aorta and the esophageal adventitia. The surface of the myocardium presented a 0.3 cm dark-red area near the apex. Additionally, the lung displayed diffuse collapse, edema, and congestion.

Figure 2. The mediastinal neoplastic mass surrounding the pericardium (arrow). Lung with diffuse collapse and congestion

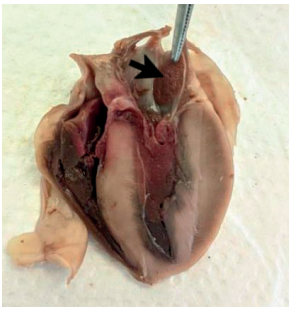

Figure 3. Four-chamber cross-section view of the formalin-fixed heart showed focal 0.55 x 0.4 cm area of endocardiosis (arrow) in the left free wall atrium

The four-chamber cross-section view of the formalin-fixed heart showed an oval 0.55 x 0.4 cm severe focally extensive area with endocardiosis in the left free wall atrium (Figure 3).

Cytological evaluation of the mass revealed a predominance of the medium-sized lymphocytes, with round eccentrically placed nuclei, centrally-placed prominent nucleoli, moderate anisocytosis, and anisokaryosis and atypical mitosis supportive of lymphoma (Figure 4).

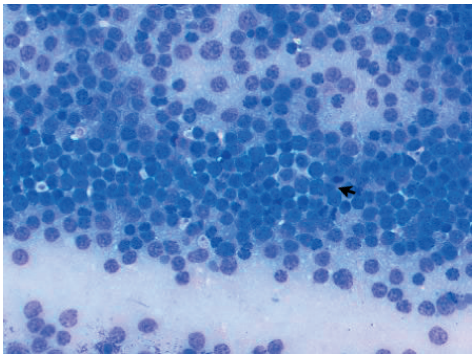

Figure 4. Medium-sized lymphocytes with round eccentrically placed nuclei, centrally-placed prominent nucleoli, moderate anisocytosis, anisokaryosis, and atypical mitosis (arrow) (MGG, ob. 40)

The histopathological evaluation of the proliferation showed a homogeneous population of round small lymphocytic cells with scant cytoplasm, and round nuclei. The nuclear size was generally 1 to 1.5 times the diameter of an erythrocyte. The number of mitoses per high-power field (400x, 0.237 mm^2 area) ranged from 2 to 10, classifying the tumor as high grade, with a total mitotic count of 54 in 2.37 mm^2 (Figure 5 A). Immunohistochemically, the neoplastic cells from tumoral mass showed an intense and diffuse reaction for CD3 monoclonal antibody, confirmed T-cell lymphoma (Figure 5 B), but no immunoreactivity with PAX-5 antibody. Based on the cytological, histological, and immunohistochemical results, the tumor was diagnosed as T-cell lymphoma, with neoplastic invasion into the pericardium and discreetly into the epicardium, anatomically classified as thymic lymphoma.

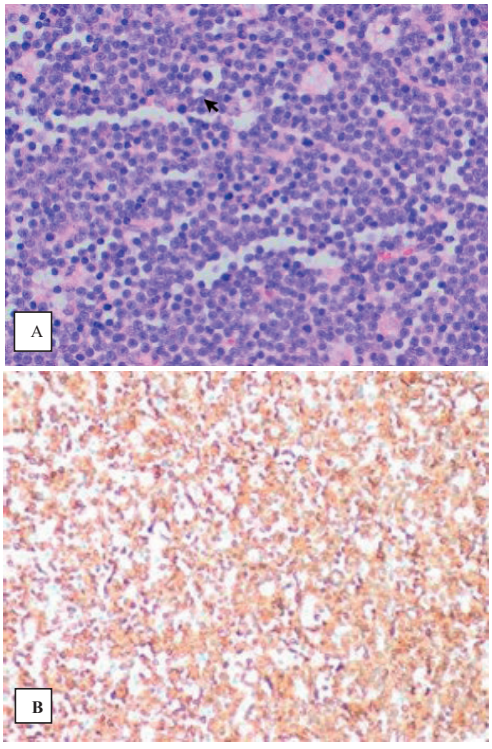

Figure 5. Histological section of feline mediastinal lymphoma, with atypical mitosis (arrow) (A) (H & E stain, ob. 10), and immunohistochemical staining for CD3 (B) (ob. 10)

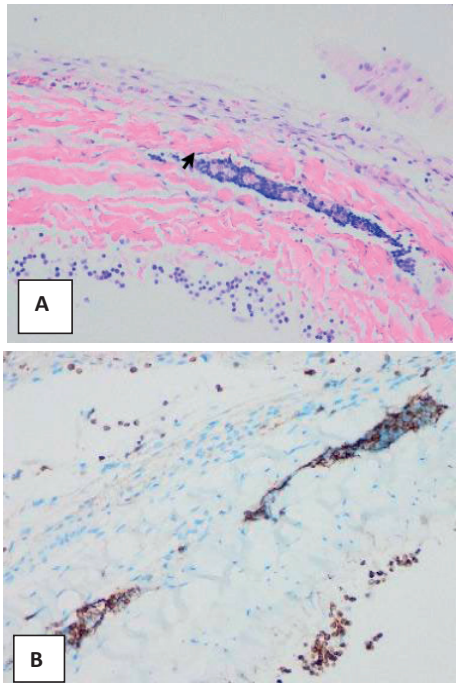

Figure 6. Pericardium with tumoral cells infiltrate (arrow) (A), showing a diffuse cytoplasmic positivity for CD3 (B) (H & E stain, ob. 20).

The pericardium showed multifocal invasion with small lymphocytic cells, with neoplastic cells diffusely expressed CD3 (Figure 6). Left atrial endocardium presented subendothelial focal thickening of connective tissue composed of dense elongated or stellate fibroblasts with elongated nuclei and pale enlarged intercellular spaces (edema) (Figure 7). At the left ventricular wall epicardium were observed discrete scattered small lymphocytic cells, among of neutrophils and degenated mesothelial cells (Figure 8 A), CD3 immunopositive (Figure 8 B), while the ventricular myocardium showed intercellular edema, cellular dilaceration, vacuolar and hyalin degeneration, and necrosis in small, isolated areas. The presence of granulation tissue, with neoformation capillaries, infiltration with small lymphocytic cells, plasma cells, and macrophages has been also identified. Additionally, the lung displayed collapse, edema and congestion.

The feline heart is a rare location for neoplasia, and less than 1% of 51,322 cats diagnosed with cancer had cardiac involvement (Kharbush, Hohenhaus, Donovan, & Fox, 2021).

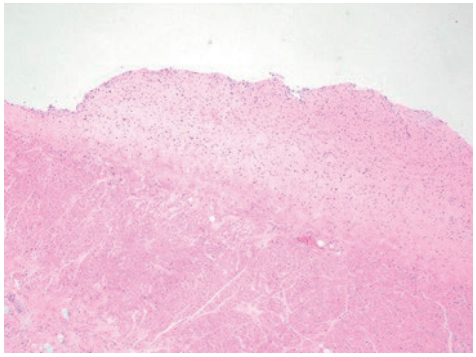

Figure 7. Endocardial fibroelastosis (H & E stain, ob. 10)

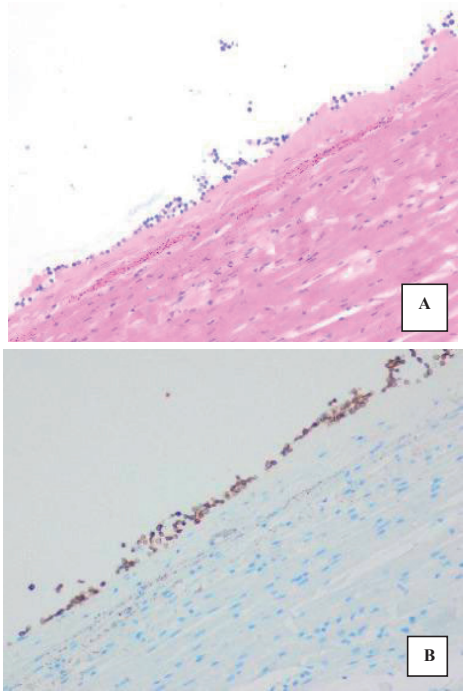

Figure 8. Epicardium with discrete tumoral cells infiltrate (A) (H & E stain, ob. 20), and neoplastic cells diffpositive for CD3 (T-cell marker) (B) (ob. 20)

Secondary cardiac involvement of lymphoma occurs more frequently than primary cardiac lymphoma, the incidence of the last being 0.03% in cats (Burgess, 2020). Metastatic tumors of the heart and pericardium appear by displacement or spread from other thoracic organs with neoplasia (Tilley, Bond, & Patnaik, 1981). In contrast with primary tumors, most metastatic neoplastic lesions reported by post-mortem (75%) are found in the inner third of the left ventricular free wall, in the

interventricular septum, or both (E. Treggiari, Pedro, Dukes-McEwan, Gelzer, & Blackwood, 2017).

According to the literature, lymphoma is the most common neoplasm in cats, occurring in 90% of feline tumors with hematopoietic origin (Sunpongsri et al., 2022; Treggiari, Pedro, Dukes−McEwan, Gelzer, & Blackwood, 2017; Twomey & Compendium, 2005). The point-of-care testing for feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) of this cat was unknown. The FeLV infection increases the relative risk 60-fold or greater; approximately 25% of cats with this virus association can develop lymphoma. FIV infection increases the relative risk of lymphoma 5-6-fold (Burgess, 2020). Cats with FeLV and FIV co-infection have a relative risk increased 75-fold (Alejandro et al., 2019).

Like in this case report, most young cats with lymphoma have T-cell positive lymphoma (Seo et al., 2006), although, in cats, B-cell lymphoma is more common than of T-cell origin (Twomey & Compendium, 2005). The age range of cats with B-cell lymphoma varied from 6 to 204 months (median of 60) and from 10 to 240 months (median 120) for cats with T-cell lymphoma (Leite-Filho et al., 2020).

In dogs, immunophenotyping is commonly used for prognostication purposes, but in cats is frequently used to confirm the presence of a phenotypically identical population of lymphoid cells (Burgess, 2020). A prognostic factor parameter is age. The cats aged under four years had shorter survival time than those over four years of age (Sunpongsri et al., 2022). Cell morphology (large cell vs. small cell) is used more commonly than a phenotypic distinction to determine treatment and prognosis.

Mediastinal high-grade lymphoma progresses rapidly; even with chemotherapy, the prognostic is poor (2-3 months) (Burgess, 2020).

The criteria of the initial diagnosis of hypertrophic cardiomyopathy (HCM) phenotype of this case report are not known. Pathological examination reveals only discreet tumoral cell infiltration at the pericardium and did not show other myocardial damage such as extended myocardial necrosis. However, neoplastic diseases such as lymphoma, myocarditis, and toxoplasma infection have been reported as myocardial diseases for differentiating hypertrophic myocardium in cats (Tanaka, Suzuki, Hirata, Kagawa, & Koyama, 2022).

Endocardial fibroelastosis (EFE) is an anomaly characterized by fibrous and elastic endocardial thickening and can be diffuse or localized. Diffuse EFE can be primary, in the absence of other important cardiac lesions, or secondary, associated with congenital cardiovascular malformations, viral myocarditis, cardiomyopathy, myocardiosis, myocardial necrosis. Localized endocardial thickening can be secondary to a multitude of myocardial injuries. Like in this case, the left side of the heart is nearly always involved (Zook & Paasch, 1982).

CONCLUSIONS

In this case, mediastinal lymphoma with pericardial invasion was diagnosed post-mortem. Based on the results, mediastinal lymphoma with cardiac involvement should be considered in young cats with clinical respiratory and cardiac signs. Mediastinal masses may be suspected basis on the physical and radiographic findings, but the final diagnosis is based on cytological, histopathological, and immuno-histochemically examination.

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