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Concurrent cardiac and splenic hemangiosarcoma with liver metastasis in a Golden Retriever

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Case presentation:

A 12-year-old, 33 kg intact male Golden Retriever presented to the veterinary clinic complaining about severe lethargy, weakness, exercise intolerance, anorexia, weight loss, and dyspnea which worsened in the last three days. No prior health issues were reported. The physical examination revealed pale mucous membranes, mild tachycardia (180 bpm), weak hypo-kinetic femoral pulses, increased respiratory effort, mild jugular distention, abdominal distention, and muffled heart sounds. The systolic blood pressure measurement was 80 mmHg Doppler (4.0 cuff dorsal pedal artery). A cardiac POCUS (point of care ultrasound) showed pericardial effusion with the diastolic collapse of the right atrium consistent with cardiac tamponade. Pericardiocentesis was performed, and 100 mL of hemorrhagic pericardial fluid was removed. (Fig 1).

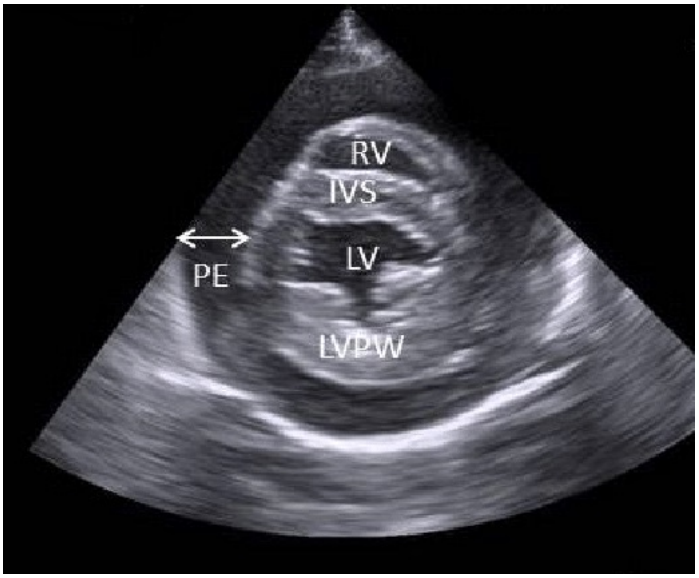

Fig. 1 Right short parasternal axis at the level of the papillary muscle. (RV-right ventricle, IVS interventricular septum, LVW-left ventricular wall, PE pericardial effusion)

After stabilizing the patient, initial diagnostic plans included in-clinic hematology and serum biochemical profiles, parasitological testing, cytology of the extracted fluid, thoracic radiographs, and echocardiography.

CBCs and serum biochemical analyses were performed. Results of the CBC revealed moderate anemia (red blood cells 3.99 x 10^{12}, normal range 5.5-8.5.0 x 10^{12}); hematocrit 21.7 %, normal range 39-56%; hemoglobin 74 g/L, normal range 110-190g/L) and mild leukocytosis 19 x 10^9 (normal range 6.0-17.0 x 10^9). Serum biochemistry showcases mild increase blood urea nitrogen concentration (BUN- 80 mg/dl, normal range < 51 mg/dl) and elevated hepatic

transaminase activity (ALT- alanine aminotransferase 190u/I, references <113u/I; AST-aspartate aminotransferase 63 u/I, references <47 u/I; ALP-phosphatase alkaline 428 u/I, references <132 u/i). Due to the high prevalence of *Dirofilaria spp*. in Romania, an Idexx Snap 4DX test was done, which confirmed the presence of parasites.

After an hour of oxygen therapy, respiratory distress decreased, blood pressure was restabilized, and an echocardiogram was performed. No pericardial effusion was seen, but a mixed echogenic mass was present in the right auricle and right atrium that continued into the right ventricle wall. It measured approximately 3 cm and occupied about 50 % of the right atrial surface (Fig.1). Moderate hypertrophy was observed in the interventricular septum and left ventricular free wall (caused by reduced preload), and concurrent myxomatous mitral valvular disease was present (Fig. 2).

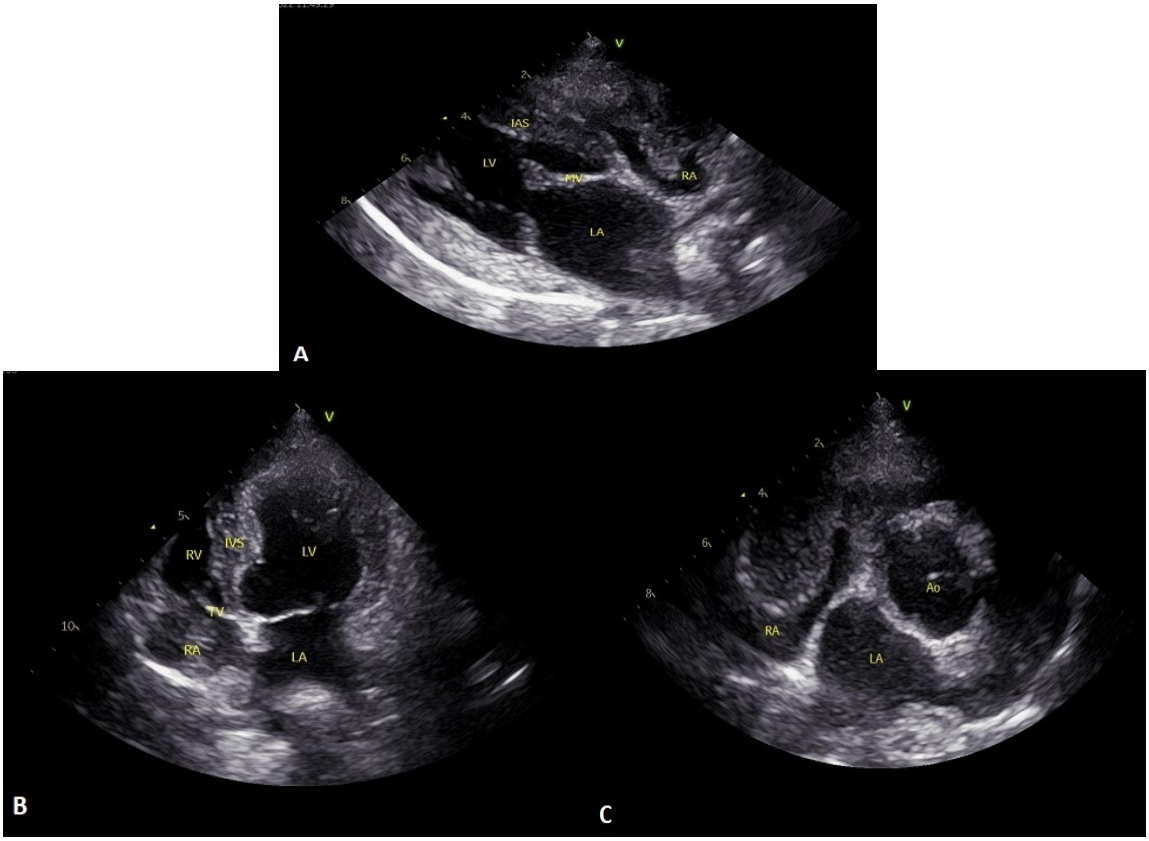

Fig. 2 A Right long parasternal axis, four chambers- myxomatous lesion on the mitral leaflet, heterogeneous mass involving the right atrium and right ventricle wall (also see in B and C); B, left long parasternal axis, the mass occupying almost all of the right atrial chamber in diastole; C, right short axis at the level of the aorta and left atrium, the atrial mass is expanding to the right ventricular chamber.

Due to the location of the tumor, the primary suspicion was hemangiosarcoma (HSA). Because one-quarter of dogs with splenic HSA have right atrial HSA, an abdominal ultrasound was performed. (6)

Ultrasound revealed splenomegaly with irregular margins, heterogeneous with multiple hypoechoic areas, and an inhomogeneous liver with multiple hypoechoic nodules. (Fig 3 A, B). Concurrent splenic hemangiosarcoma was suspected.

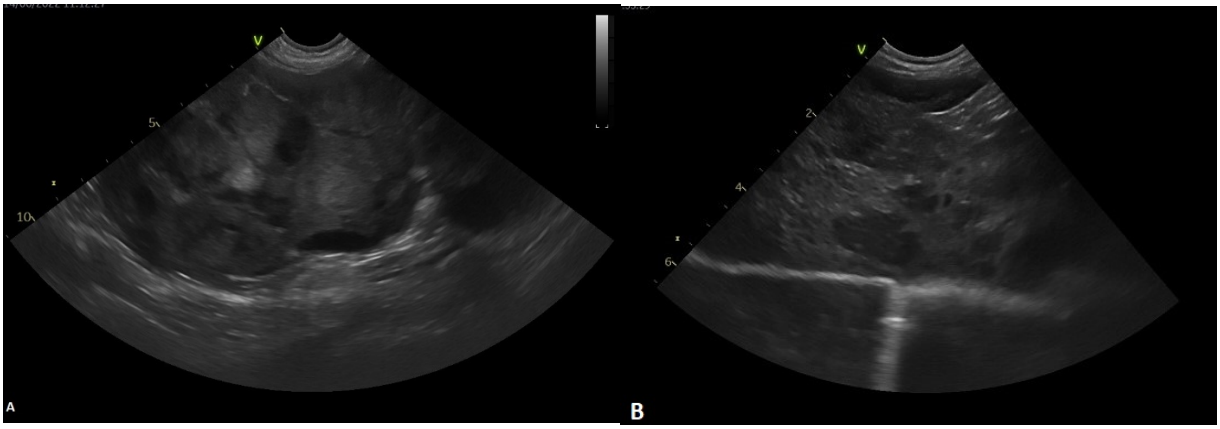

Fig. 3A Enlarged spleen, inhomogeneous, with hyperechoic areas which interfere with hypoechoic/anechoic areas; B, inhomogeneous liver, hyperechoic with hypoechoic nodules with different dimensions.

Thoracic radiographs revealed a normal cardiac silhouette (after pericardiocentesis) and no sign of metastasis. (Fig. 4)

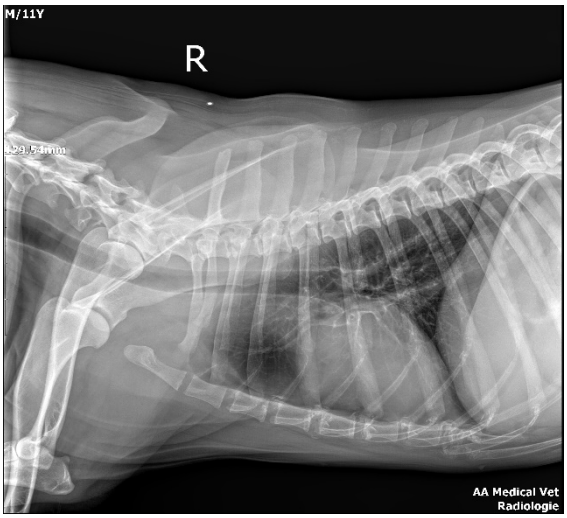

Fig. 4

By the time of diagnosis, the tumor had likely metastasized to the liver, which led the owner to choose between palliative treatment or chemotherapy after a confirmatory biopsy. Due to the recurrence of cardiac tamponade, which typically recurs within a few days, the owner was informed of the likelihood of disease progression despite treatment and elected humane euthanasia. A gross necropsy was performed.

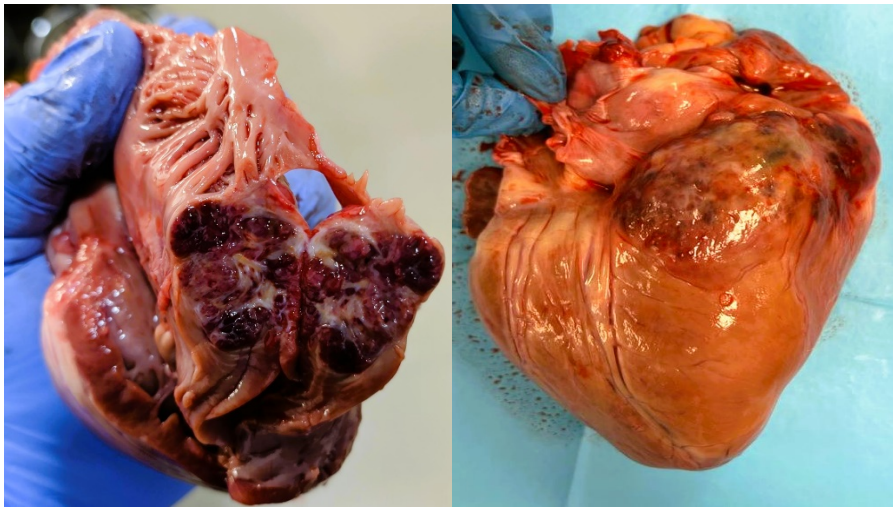

Fig. 6 (A, B) The right atrial mass bulged beyond the epicardium, encroaching the RA cavity.

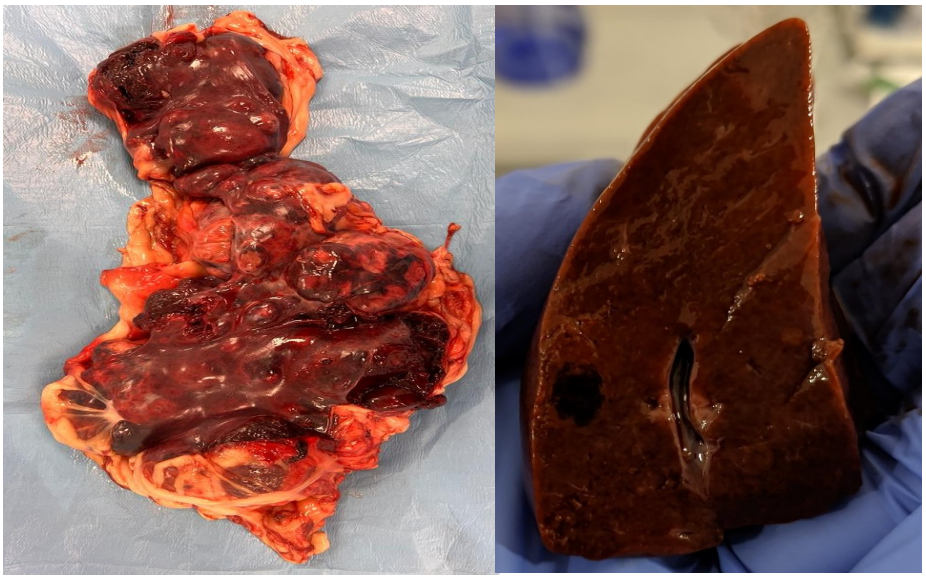

Fig 7 A Enlarged spleen with irregular contour and disseminated reddish black and white nodules with necrotic areas on its surface, with mesenteric fat attached; B, a section of the liver- dark red nodule is seen in the parenchyma.

The owner approved a histopathological exam for confirmatory diagnosis, and the heart, spleen, and liver were submitted to a specialist laboratory.

Histopathological exam of the liver revealed multiple tumor formations of variable sizes, 3 - 12 mm in diameter, the small infiltrative ones among hepatocytes. Tumor cells have indistinct borders, little cytoplasm, oxyphil, round, oval nucleus, finely granular chromatin, 1-3 punctate nucleoli, basophils, moderate anisokaryosis, and 15 mitosis/10 hpf. The vascular spaces are occasionally dilated by an amorphous, pale oxyphilic material and degenerated red blood cells. Hepatocytes in the adjacent parenchyma show cytoplasm occupied by large optically empty vacuoles (macro vacuolar steatosis), and sinusoidal capillaries are occasionally dilated. (Fig.8C)

Splenic parenchyma showed multiple circumscribed nodular formations, not encapsulated, occasionally infiltrative in the adjacent splenic parenchyma, with cellularity and architecture similar to liver masses, occasionally with areas of hemorrhage, with variable, fine to moderate connective stroma. Cells tumors show identical morphology, with moderate to severe anisokaryosis and anisocytosis, with 24 mitoses/10 hpf. Intratumoral vessels are large and infiltrated in middle numbers by plasma cells, lymphocytes, and neutrophils. The red pulp is severely congested, infiltrated by numerous plasma cells, small lymphocytes, hemosiderophages, and cellular elements of extramedullary hematopoiesis. (Fig.8B)

Myocardium infiltrated by a tumor proliferation made up of mesenchymal cells that form irregular vascular spaces, small in size, with capillary, with rare solid areas, with fine connective stroma, occasionally moderate, with dense bands of collagen, and abundant stroma in the central location, with reduced cellularity or acellular, with areas of hemorrhage (ischemic necrosis). Proliferation nodules are present in the subepicardial adipose tissue with infiltrative growth among adjacent adipocytes and myocardiocytes. Tumor cells have similar morphology to previously described in hepatic and splenic tumors, with moderate anisokaryosis, 21 mitoses/10 hpf. Tumor stroma, adjacent myocardium, and subepicardial adipose tissue are infiltrated by solitary tumor cells or arranged in nests, frequently perivascularly. Focally, the endocardium of the right ventricle is eroded and infiltrated by tumor cells. Multifocal, intratumoral, reduced areas of necrosis are present, infiltrated by neutrophils in moderate numbers, rare lymphocytes, and macrophages. (Fig.8A)

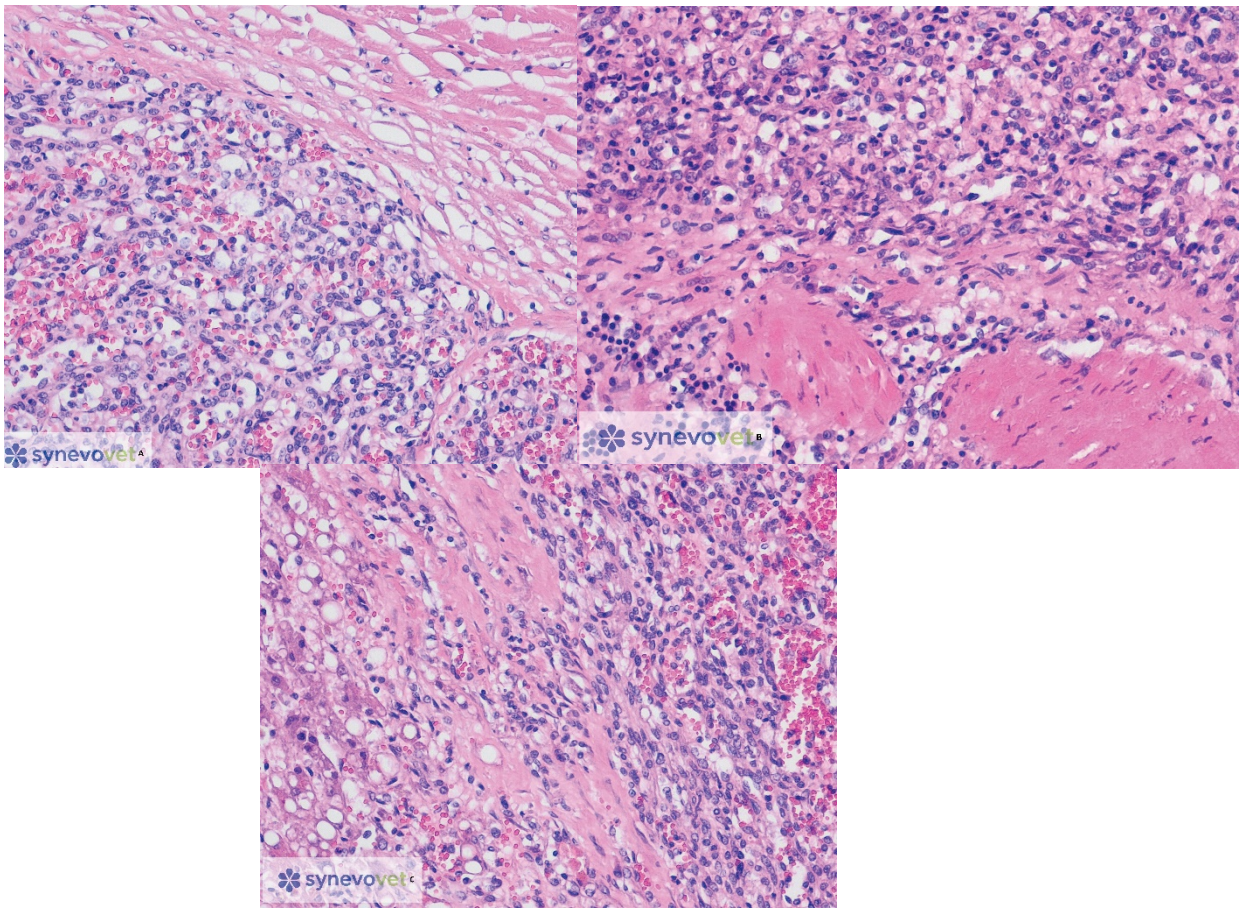

Fig. 8 A, histopathological aspect of the cardiac hemangiosarcoma; B, histopathological part of the splenic hemangiosarcoma; C, histopathological aspect of the liver hemangiosarcoma

The histopathological exam confirms the diagnosis of splenic and cardiac capillary type hemangiosarcoma with liver metastasis.

Discussion:

Hemangiosarcoma is an aggressive malignant neoplasm that arises from either the vascular endothelium or endothelial precursor cells. In recent years, studies suggest a pluripotent bone marrow progenitor as the cell of origin for this disease. More recent data sustain that some genes like pro-inflammatory genes, endothelial cell-matrix interaction genes, and pro-adipogenic and connective tissue-forming reflect the composition of the tumor microenvironment, and the tumor microenvironment enhances tumor growth and survival or promotes the migration of tumor cells. (7)

The most common places of origin are the spleen, right atrium and auricle, subcutaneous tissues, and liver. However, because this tumor originates from vascular endothelial cells, it can arise in any tissue or organ containing vascular structures: bone, bladder, aorta, prostate, muscle, lungs, oral cavity, kidneys, and uterus. (5) This tumor metastasizes quickly to distant organs via hematogenous routes due to readily access to the systemic circulation. Metastasis commonly occurs in the lungs (the most frequently affected site) and liver via hematogenous metastasis and the omentum/mesentery via direct implantation due to rupture of a splenic or hepatic HSA. Visceral HSAs are more common than cutaneous HSAs and are associated with a poorer prognosis. (7)

The etiology remains incompletely understood and occurs more frequently in dogs than in other domestic animals. The tumor occurs most frequently in older dogs (more than ten years old). Manifestation of the tumor exhibits no breed or gender preferences, although reports suggest higher prevalence in large-breed dogs such as German Shepherds and Golden Retrievers. In Golden Retrievers, a set of hemangiosarcoma-associated genes suggests these are modulated by (or with) heritable traits that may influence the risk for this cancer. (3)

Morphologically, they can have a capillary, cavernous, or solid appearance, and the malignant cells can be highly pleomorphic with features reminiscent of those seen in other sarcomas. Hemangiosarcoma is observed in 0.3 to 2% of all canine necropsies, constitutes about 5% of all malignancies in dogs (5), and is the most common type of malignant cardiac tumor in dogs (approximately 70% of cardiac neoplasms in dogs). (2) The prognosis of cardiac hemangiosarcoma is poor, due to its highly invasive nature, with a reported median survival time of 7 days in non-treated dogs, between 42 days and five months in dogs with surgical removal of the tumor, only 139 days in dogs with chemotherapy, and between 175 days and 189 days in dogs with surgical removal of the tumor and conventional chemotherapy. (1,2)

In a retrospective study including 54 dogs, Golden retrievers were found to be 10.56 times more likely to have a concurrent cardiac mass when presenting for signs associated with a splenic HSA. (4). In another study, one-quarter of dogs with splenic HSA have right atrial HSA. (6)

Conclusion:

In the present case, the localization of the formation at the level of the right atrioventricular myocardium may be primary. Still, the development cannot be excluded entirely to be secondary following metastasis from the splenic level. In the case of hemangiosarcoma metastases to the heart, they can be located at the ventricular or atrial level.

Dogs with a potential hemangiosarcoma must have complete staging using three orthogonal thoracic radiographs, abdominal ultrasound, and echocardiography to assess the right side of the heart. Those are recommended due to the predisposition for widespread metastasis.

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Hpf (high power field),