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Case Report

Concomitant occurrence of multicentric hemangiosarcoma and histiocytic sarcoma in a dog

Bethânia Almeida Gouveia[1]*, Isabela Fernanda Spinelli Perossi[1], Marina Carla Bezerra da Silva[1], Paulo Edson Baptista Martinelli[1], Fernanda Ramalho Ramos[1], Andrigo Barboza De Nardi[2], Rosemeri de Oliveira Vasconcelos[3].

[1] Programa de Residência em Área Profissional da Saúde – Med. Vet. e Saúde, Faculdade de Ciências Agrárias e Veterinárias (FCAV), Universidade Estadual Paulista (UNESP), Campus de Jaboticabal, SP, Brazil.
[2] Departamento de Clínica e Cirurgia Veterinária (FCAV-UNESP), Jaboticabal, SP, Brazil.
[3] Departamento de Patologia, Reprodução e Saúde Única (FCAV-UNESP), Jaboticabal, SP, Brazil.

***Corresponding author:**bethania.gouveia@unesp.br

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Abstract

Histiocytic sarcoma (HS) is uncommon malignant neoplasia of round cells with marked predilection in Rottweiler and Bernese Mountain. The disseminated form, which mainly affects the spleen, lungs, lymph nodes, bone marrow, skin, and subcutis, presents a quick and aggressive clinical behavior. Hemangiosarcoma (HAS) is a malignant neoplasm of endothelial vessel cells commonly reported to affect the right atrium of dogs' hearts. A male Rottweiler, five years old, presented flaccid paraplegia and progressive muscular atrophy in the temporal, masseter, and limbs muscles; Due to the clinical stage of the animal, euthanasia was conducted. During the necroscopic examination, it was noticed that several masses presented different sizes; some were whitish, and others were reddish and spread in multiple organs (lungs, heart, spleen, stomach, kidneys, brain, medulla, skeletal muscle, and pre-scapular lymph node). Microscopically, in some organs such as the stomach, right ventricle, lungs, and medulla, it was noticed a proliferation of myeloid cells, highly cellular, with poor demarcation, no encapsulation, and with the infiltrative growth pattern of cells with high pleomorphism. Numerous tumoral emboli were observed in the spleen, brain, skeletal muscle, and lymph node. These cells were submitted for immunohistochemistry and were positive for CD18 (HS antibody). In the right atrium, liver, and kidney it was observed malignant and infiltrative endothelial proliferation (HSA) and emboli in the medulla. Therefore, we conclude that both neoplasms (HS and HSA) cause the animal's paraplegia due to their embolism and metastasis to the spinal cord and skeletal muscle.

Key words: mesenchymal neoplasia. paraplegic, metastasis, round cells.

Introduction

Histiocytic sarcoma (HS) is a malignant neoplasm of histiocytic origin (macrophages and dendritic cells), there is low frequency, but most cases are in dogs (2, 18). Rottweiler and Bernese Mountain breeds are the most described (1). Generally, the affected animals are middle-aged to older, the clinical symptomatology is unclear, and the animals present lethargy, anorexia, and weight loss. Other clinical signs appear according to the organ affected by neoplastic nodular formation (18). Most histiocytic disorders in dogs and cats are related to the proliferation of Langerhans cells or interstitial dendritic cells, and only hemophagocytic histiocytic sarcoma is of macrophage origin (2, 5, 11, 17).

HS can present in a localized or disseminated form; the disseminated form affects different sites (12). Sites frequently affected are spleen, lung, lymph nodes, bone marrow, skin, subcutaneous tissue, liver, periarticular and articular tissues. The central nervous system is less affected (2, 6, 16).

Hemangioma (HA) and hemangiosarcoma (HSA) are neoplasms derived from the disorganized proliferation of endothelial cells in blood vessels, with hemangioma being the benign form and hemangiosarcoma the malignant one (13). Dogs with hemangiomas are younger when compared

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to those with hemangiosarcoma (22), and the animals affected by these neoplasms have an average age of 9.3 years (21).

The etiology of HSA is not well understood, although, in dogs, it is suggested that short-haired or poorly pigmented animals, when excessively exposed to the sun's ultraviolet rays, have a greater chance of developing the disease (6, 8, 24).

HSA is reported more frequently in dogs when compared to other species (4) and are characterized by rapidly developing metastases and aggressive behavior (21). Furthermore, it was observed that 55% of 40 HSA cases were multicentric. Multicentric HSA is one that affects several organs, making it impossible to establish their primary site, and in most cases, this tumor behavior originated from the metastatic process (10).

The clinical signs of this type of tumor vary according to its anatomical location and the highly vascularized nature of the tumor, which can rapidly spread through the hematogenous and lymphatic pathways, progressing to metastasis in almost all organs, especially the lung (4). Therefore, the objective of this case report was to describe the simultaneous occurrence of HS and HSA in a dog with systemic involvement and locomotor impairment.

Case description

A five-year-old male Rottweiller dog arrived at the small animal surgery sector of FCAV - UNESP, Campus de Jaboticabal, in January 2019, for treatment of paraplegia and muscular atrophy of the pelvic limbs, masseter, and temporalis muscles. The animal had a history of hind limb paresis for three months and worsening in the last 15 days. In addition, the animal presented its head tilted to the right side (head tilt) two days after the consultation. The animal also had a capricious appetite and presented with pathological vertical nystagmus during the neurological examination.

Additional tests were performed, such as complete blood count (CBC), biochemical measurements, and radiography of the spine at cervical and thoracolumbar height with latero-lateral and ventro-dorsal projections. The CBC showed elevated mean corpuscular hemoglobin (MCH) and leukocyte levels in the blood. Serum biochemical analysis showed an increase in urea, and globulin, a decrease in albumin, and a marked increase in the enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and creatine kinase (CK). Imaging studies suggested intervertebral disc disease and spondylosis. The clinical suspicion was myopathy.

Without any expectation of clinical improvement, the patient was euthanized. The animal was referred to the Animal Pathology Service of the same institution for necroscopic examination, with evaluation and photographic documentation of macroscopic alterations and collection of material for histopathological examination.

During the necroscopic examination, the lungs were diffusely reddened and showed multifocal, blackened, smooth nodular areas that measured approximately 1.5 cm in diameter (Fig. 1A). In the left atrium, three whitish areas measured 0.2 cm, 1.0 cm, and 0.3 cm in diameter and were homogeneous and

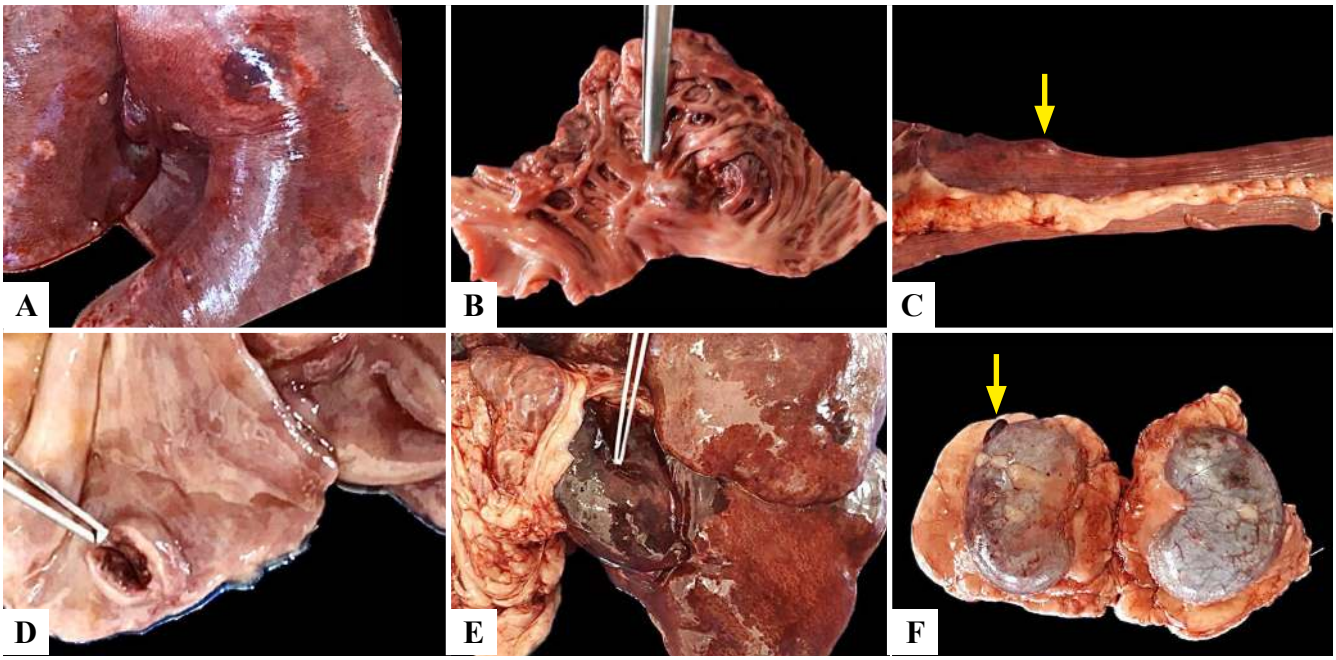


Figure 1. Macroscopic appearance of a dog's organs with HS and HSA. **A.** Lung with the presence of a flat nodule, approximately 1.5 cm in diameter, soft and blackish (arrow). **B.** Nodule in the left atrium, approximately 1.0 cm in diameter and whitish (tip of the forceps). **C.** Spleen with soft nodulation near the edge, approximately 0.5 cm in diameter (arrow). **D.** Gastric mucosa with a firm nodule measuring 1.8 x 0.1 cm, with a reddish and homogeneous surface when cut (tip of the forceps). **E.** Liver with the presence of a mass measuring approximately 8.0 x 4.0 cm in the right medial lobe, red-black and soft (tweezers tip). **F.** Kidneys showing in the left renal capsule a nodule measuring 1.5 cm in diameter, reddish and soft (arrow).

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whitish on cutting (Fig. 1B). At the apex of the heart, between the left and right ventricles, there was a soft, whitish nodule that measured approximately 1.0 cm in diameter. There were several reddish nodules in the omentum, each about 1.0 cm in diameter and a whitish nodule 4.0 cm in diameter.

The spleen had rounded edges (moderate increase in volume), was diffusely dark red, and had multifocal blackened areas located mainly near the edges. The largest one was 0.5 cm in diameter (Fig. 1C). A firm nodule measuring 1.8 x 0.1 cm in the stomach that, when cut, had a reddish homogeneous surface (Fig. 1D). The liver was markedly enlarged, diffusely red, and with an evident lobular pattern. On cutting, multifocal black areas were observed where a discrete amount of blood flowed (Fig. 1E). The renal capsular surface had reddish areas measuring approximately 1.5 x 1.0 cm (Fig. 1F). Similar lesions were observed in the perirenal fat. In addition, there was a blackened punctiform lesion measuring 0.2 cm in diameter in the renal cortical region.

Microscopically, in the stomach submucosa, there was a locally extensive area of neoplastic proliferation of malignant mesenchymal cells, with a myeloid, highly cellular, poorly demarcated, non-encapsulated, infiltrative growth, and high pleomorphism. The nuclei were round, paracentral, with finely clustered chromatin. Nucleoli, on the other hand, were evident and sometimes doubled. In addition, marked anisocytosis, anisokaryosis, karyomegaly, and sometimes multinucleated cells were observed.

The histological sections embedded in paraffin were sent to a private laboratory for immunohistochemistry to confirm the origin of the tumor cells. The neoplastic cells were positive for CD18 antibodies (a marker of histiocytic neoplasms), HLA-DR (Major histocompatibility complex MHC II), and Lysozyme (a marker of granulocytes, histiocytes, and myeloid leukemias). However, when subjected to lymphoid cell markers (CD3 and CD20), the result was negative, confirming its origin and the diagnosis of histiocytic sarcoma (Fig. 2).

Metastases were visualized in the spinal cord (Fig. 3A and 3B), lung (Fig. 3C), cardiac ventricle, as well as neoplastic emboli in the spleen, brain, and leptomeninges, kidney, skeletal muscle, and lymph node (Fig. 3D).

Concomitantly, in the right atrium, there was a densely cellular, poorly demarcated, non-encapsulated, growing infiltrative proliferation of malignant mesenchymal cells that differed histologically from HS. The cells form rudimentary vascular spaces filled with blood, have indistinct shapes and boundaries, and moderate and weakly eosinophilic cytoplasm. The nuclei were oval, paracentral, with finely clustered chromatin and inconspicuous nuclei. There were also rare binucleated cells. The characteristics of this neoplasm led to the diagnosis of hemangiosarcoma. Metastases were evident in the mesentery, liver, kidney, and intestine. Neoplastic emboli were seen in vessels of the spleen and spinal cord (Fig. 3E and 3F).

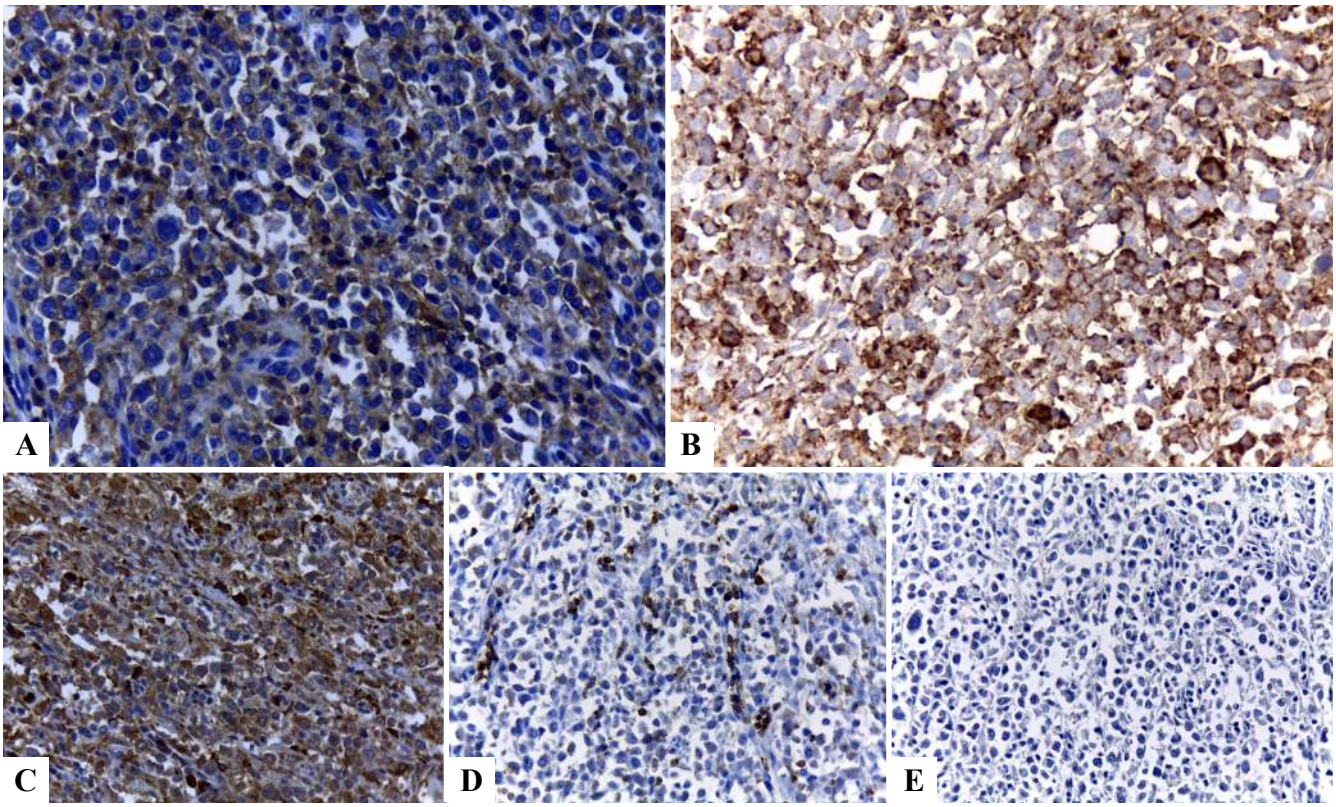


Figure 2. Panel of immunohistochemical markers for tissues from dogs with SH. **A.** Positive staining for CD18 in neoplastic cells, objective 20X. **B.** Positivity of tumor cells for MHC II, objective 20X. **C.** Lysozyme-positive tumor cells, 20X objective. **D.** Negative labeling of tumor cells for CD3, 20X objective. **E.** Negative labeling of the tumor for CD20.

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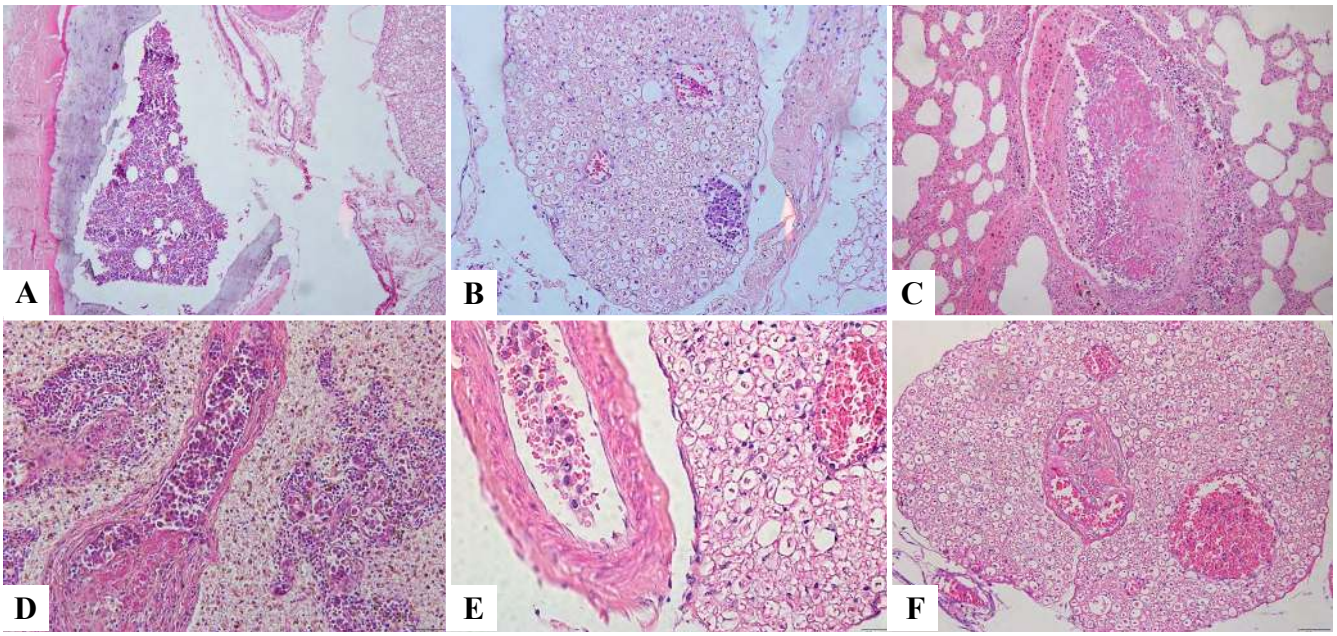


Figure 3. Photomicrographs of different organs in a dog with HS and HSA metastasis and embolism. **A-B.** Spinal cord, lumbar region. Note the presence of neoplastic myeloid cells (HS) invading blood vessels, 10x objective. **B.** Spinal cord with an area of neoplastic myeloid (SH) cell metastasis in adjacent nerves, 20x objective. **C.** Lung, with a focal area of SH perivascular metastasis, 10x objective. **D.** Lymph node, showing multifocal areas of metastasis of neoplastic myeloid cells in the spinal cord. **E.** Invasion of neoplastic mesenchymal cells is observed in a blood vessel (HS). **F.** Focal area of HSA metastasis in the spinal cord. Hematoxylin and Eosin.

Discussion

Histiocytic sarcoma is a neoplasm that mainly affects elderly dogs, as reported by Oliveira et al. (20). This author observed this neoplastic type in dogs ten years of age. Moore (17) reported a range between two and 13 years of age, agreeing with the animal's age in this study.

According to Takada et al. (25), the breeds most affected by HS are Bernese Mountain, Flat-coated Retriever, Golden Retriever, German Shepherd, and Rottweiler. In a study by Dervisis et al. (9), eight of 36 animals with HS were of the Rottweiler breed.

HS is either localized or disseminated (16). The localized form of HS often presents as a cutaneous nodule, while metastases usually occur in peripheral lymph nodes (2,14). In the present report, the disseminated form of the neoplasm was observed.

The disseminated form of HS affects different sites such as the spleen, lung, lymph nodes, and the central nervous system, as well as occurs in the present report. However, bone marrow, skin, subcutaneous tissue, liver, periarticular and joint tissues are also sites that can be affected by this neoplasm (16). Oliveira et al. (20) also noted the presence of HS in the left pelvic limb, the middle third of the caudal thigh region, left axillary and inguinal lymph nodes, and metastases near lumbar and sacral vertebrae.

The macroscopy of this neoplasm varies. It can present as single nodules or plaque tumors, as Oliveira et al. (20) observed. In this report, several widespread distributed nodules were described, with variations in size, and whitish, as described by Hendrick (14), who states that the color can vary from yellowish to whitish. The size can vary and sometimes even reaches 10 or 13 cm in diameter (20).

HS can be confused with spindle cell sarcomas of different lineages (2). The diagnostic confirmation of HS should occur from the determination of the cellular origin of the tumor. Immunohistochemical analysis shows negative staining for lymphoid markers and positive for CD18 and more specific dendritic markers such as CD1, CD11c, and MHC II (14,18).

As for HSA, this neoplasm most often affects elderly dogs, with a mean age of 8.24 years (3, 24). There is controversy in the literature about the sex predisposition of HSA. Soares et al. (24) noted that females were more affected than males. However, Schultheiss (22) reported that males were more affected, corroborating what was described in the present report.

According to Berselli et al. (3) and Soares et al. (24), the breed most affected by HSA is the pit bull. Goldschmidt and Hendrick (2002) correlated a greater involvement of this neoplasm with light-skinned animals, different from what was described in this work since the animal had dark skin. Another point to be considered is that, according to the literature, large dogs are more susceptible to developing HSA (22,23).

Flores et al. (10) and Soares et al. (24) also observed the presence of HSA in organs such as the spleen, kidney, liver, and heart, as well as in this study. In addition, the presence of HSA has been recognized in the peritoneum, pancreas, lungs, eyes, brain, and pleura (10,24). In addition, Martins et al. (15) also describe the presence of metastatic HSA in the spinal cord. The animal in the present study had hemangiosarcoma disseminated by several organs, thus, it was not possible to establish a primary anatomical site, being classified as a multicentric HSA, as described by Flores et al (10).

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Conclusions

It is concluded that the HSA and HS neoplasms led to this symptomatology involving the spinal cord and skeletal muscles. In addition, the patient had neurological signs, such as head tilt and vertical nystagmus, which is explained by the presence of neoplastic SH emboli in the brain. The described case of concomitant HSA and HS in the same patient with multiple metastases demonstrates that neoplasms can co-occur, even in young animals, which makes better oncological follow-up and monitoring necessary. Furthermore, this report highlights the importance of immunohistochemistry as a complementary tool in diagnosing neoplasms in companion animals.

Conflict of Interest

The authors declare no competing interests.

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