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Case Report

Disseminated histiocytic sarcoma in a Labrador retriever in Brazil

Saulo R. F. Gonçalves[1*], Mariana L. M. Barretto[1], Débora M. S. da Silva[2], Pedro P. F. de Albuquerque[1], Alessandra V. de Barros[2], Letícia M. Bezerra[2], Almir A. S. Filho[1], Edna M. S. Santos[2], Andrea A. F. Oliveira[1], Francisco A. L. Souza[3]

[1]Área de Patologia Animal, Departamento de Medicina Veterinária, Universidade Federal Rural de Pernambuco, 52171-900, Recife, Pernambuco, Brazil.
[2]Área de Clínica Médica de Pequenos Animais, Departamento de Medicina Veterinária, Universidade Federal Rural de Pernambuco, 52171-900, Recife, Pernambuco, Brazil.
[3]Departamento de Histologia, Departamento de Morfologia e Fisiologia Animal, Universidade Federal Rural de Pernambuco, 52171-900, Recife, Pernambuco, Brazil.
[*]**Corresponding author:** Área de Patologia Animal, Departamento de Medicina Veterinária, Universidade Federal Rural de Pernambuco, 52171-900, Recife, Pernambuco, Brazil. Phone: 55-81-3320-6420. E-mail: saulofelix.vet@gmail.com

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Abstract

Histiocytic sarcoma (HS) refers to a rare neoplasm of round cells frequently presented in a disseminated form, affecting bones, joints, skin, and subcutaneous tissue. The objective of this study was to report a case of disseminated HS in a canine attended at HOVET-UFRPE, Recife, Brazil. Physical examination and complementary tests were performed; complete blood count and serum biochemistry were normal, but at thoracic radiography exam a neoformation was detected in the right lung. Cytopathological evaluation was suggestive of malignant epithelial neoplasia. At necropsy, there were disseminated nodules in the lungs, liver, spleen, kidneys, meninges and eye. The histopathological examination revealed proliferation of pleomorphic round cells, suggesting HS, which was confirmed by immunohistochemistry. From the obtained results, it becomes evident the importance of complementary exams to properly diagnose histiocytic diseases. This is one of the few reports of canine disseminated HS in Brazil.

Key words: canine, histiocytic disease, neoplasia, histopathology, immunohistochemistry.

Introduction

Histiocytic sarcoma (HS) is a rare round cell neoplasia with poorly understood etiology, which may be presented in localized or disseminated forms, and commonly affects the bones, joints, skin and subcutaneous tissues. While it may affect dogs of any breed, the most predisposed breeds are Labrador retriever, Bernese Mountain Dog, Rottweiler, Golden Retriever, and Flat-Coated Retriever (1, 8, 12).

Clinical signs of HS vary depending on the location of the lesions and development of metastases (1). It is diagnosed by cytological and histopathological examinations and may require immunohistochemistry in order to confirm the findings on affected tissues (2).

Once diagnosed, the treatment is generally based on chemotherapy, but responsiveness is poor (5). The prognosis is generally poor but may be favorable when early diagnosed; the overall survival of three months can be achieved in patients presenting the disseminated form (11). This paper aims to report a case of disseminated HS in a Golden Retriever dog in Recife, Pernambuco, Brazil.

Case Report

A seven-year-old, 30 kg, male, Labrador retriever was presented to the Veterinary Hospital of the Federal

Rural University of Pernambuco (HOVET-UFRPE), Recife-PE, Brazil, in poor neurological condition. The owner reported two seizures episodes one week prior to the presentation and the dog had been treated by another veterinarian with phenobarbital (2.5 mg/kg,BID) and prednisolone (1 mg/kg SID for 7 days). A physical examination was performed and complementary testing including a complete blood count (CBC), serum biochemistry profile (ALT, albumin, creatinine, and urea) and thoracic radiography were requested.

On physical examination, cardiorespiratory parameters, rectal temperature and abdominal palpation were normal, as were the complete blood count and serum biochemistry profiles. Thoracic radiography revealed interstitial and bronchial opacification in the caudal pulmonary fields, and two areas of opacification in the right hemithorax suggesting a neoformation (Fig. 1A); cytopathological examination was requested.

The cytopathological examination was performed for the pulmonary neoformations via ultrasound-guided fine-needle aspiration cytology. The results were suggestive of malignant epithelial neoplasia. Phenobarbital therapy was continued, and omeprazole (1 mg/kg SID) and firocoxib (5 mg/kg SID) were additionally prescribed. Thirty days after first examination, the patient was presented for reevaluation, and radiographic and hematological exams were repeated. On radiographic images, the neoformations did not present any increase in their size and CBC was unchanged; physical evaluation revealed respiratory distress. A computed tomography was recommended but not performed. Three months after initial evaluation, the patient was presented with clinical signs of lethargy, uveitis and hypophagia, and died right after consultation.

At necropsy, white-colored fibroelastic multifocal nodules were observed in all lung lobes (Fig. 1B), as well as in the cut surface of the liver, kidneys (Fig. 1C), and spleen. Upon examination of the intracranial structures, a similar nodule was noted in the dura mater near the occipital region; an intraocular white and rubbery mass was also detected (Fig. 1D). Fragments were collected and fixed in 10% formalin, routinely processed and stained with hematoxylin and eosin.

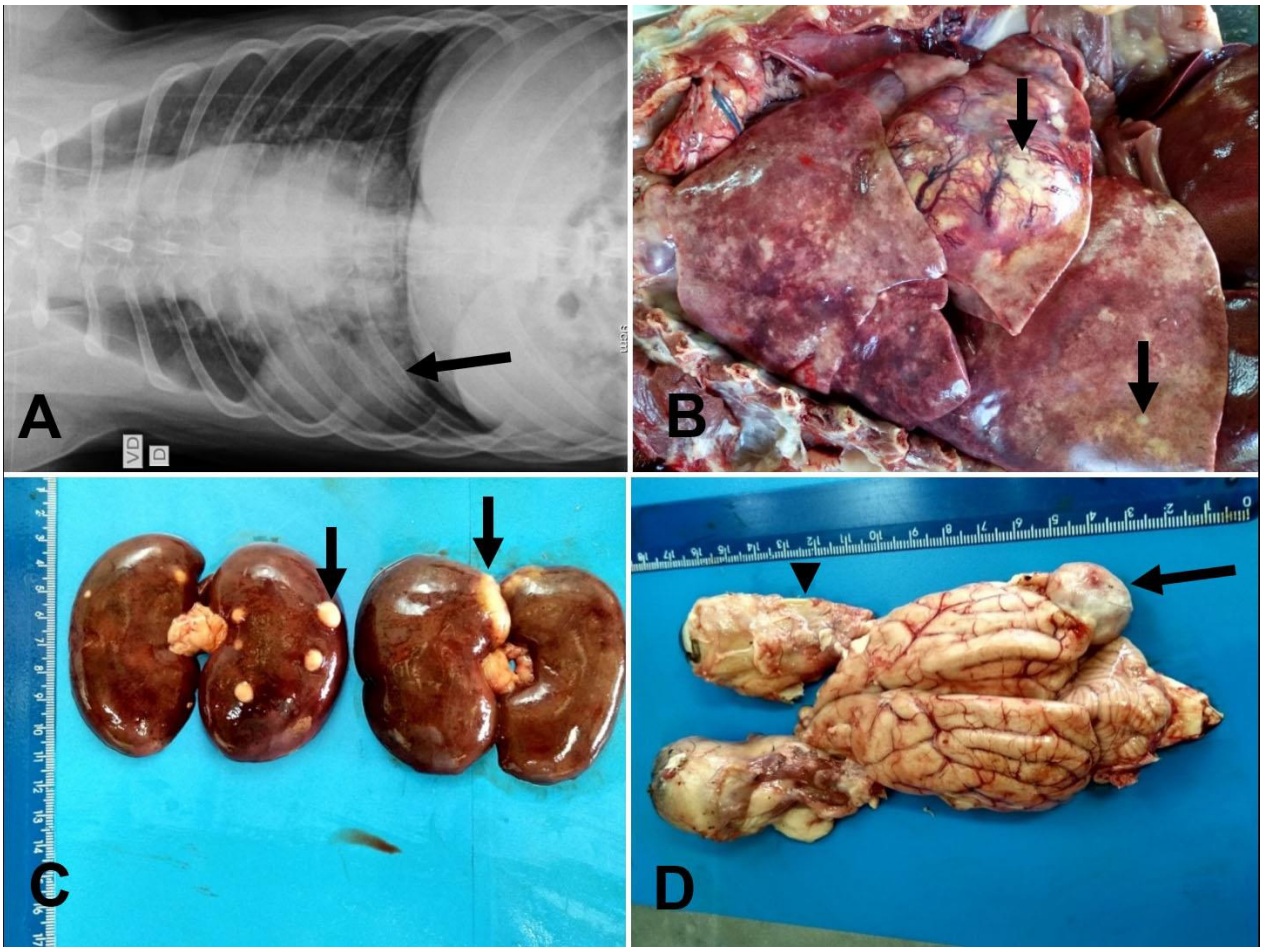

Figure 1. Radiographic and necroscopic examinations, canine, histiocytic sarcoma. **A.** Presence of radiolucent structures in caudal lobe of the right lung (arrow) suggesting neoplasia. **B.** Lung. Whitish multifocal nodules (arrow). **C.** Kidneys. Multifocal to coalescent nodules (arrow). **D.** Brain. White nodules in the meninges (arrow) and in the intraocular structures (arrowhead).

Histopathology revealed an expansive, unencapsulated, poorly demarcated proliferation of loosely clustered polygonal to round cells; they presented abundant eosinophilic cytoplasm, of undefined limits and vacuolated aspect; oval and paracentral nuclei with sparse chromatin and an evident pleomorphic nucleolus. There was a high degree of anisocytosis, anisocaryosis and nuclear pleomorphism, besides frequent karyomegaly and a large number of binucleated cells, multinucleated giant cells and mitotic figures (>10/HPF at 40x magnification); extensive necrotic zones were also observed. These results were most suggestive of HS (Fig. 2A). Immunohistochemical staining was performed for CD3, CD20 (to rule out anaplastic lymphoma), CD18 and MHC II (for cells of histiocytic origin). The samples tested were negative for CD3 and CD20 (Fig. 2B), but showed strong labeling for CD18 and MHC class II (Fig. 2C and D), confirming the diagnosis of HS.

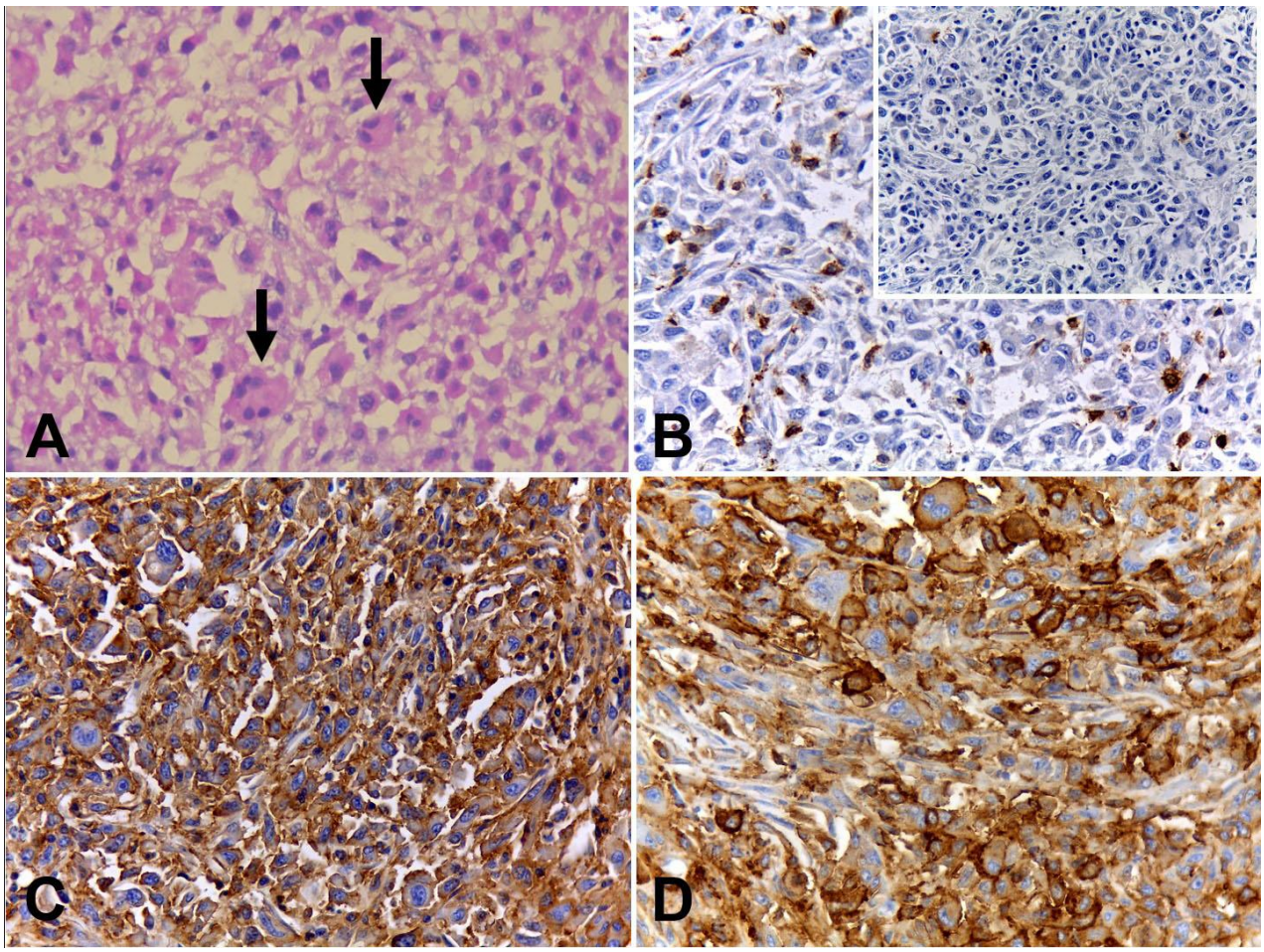

Figure 2. Histopathological sample, canine, lung, histiocytic sarcoma. **A.** Intense proliferation of pleomorphic round cells with multinucleated cells (arrow). (HE, 400x). **B.** Immunohistochemistry for CD20 (upper right image) and CD3. Positive for infiltrative lymphocytes and negative for neoplastic cells. (400x) **C.** Immunohistochemistry reveals strongly marked CD18. (400x) **D.** Immunohistochemistry reveals strongly marked MHC II. (400x).

Discussion

As observed in literature, the etiology of canine HS is still unknown (1, 8). It has been theorized that the prolonged use of anti-inflammatory drugs may cause genetic mutations and consequently develop the disease; however, further studies are needed to accurately determine its etiology (10). Adult and geriatric patients are most frequently affected and Labrador retrievers are one of the most predisposed breeds, which is consistent to this report's findings (6).

HS is rarely reported in the literature. Studies show a low incidence compared to other neoplasms, whether dermal or other presentation (2, 8). There is no sex predisposition noted to date. Clinical signs are variable, depending directly on the organs affected; generalized clinical signs include anorexia, weight loss and lethargy. Cough and dyspnea are common when there is lung involvement; in cases with central nervous system involvement, seizures, ataxia and paralysis may be observed (7). These clinical signs were demonstrated by the patient in this study. Animals with HS normally present

regenerative anemia with thrombocytopenia, elevated liver enzymes, hypoalbuminemia and hypocholesterolemia (11, 8). Since there was no bone marrow impairment by the neoplasia, hematologic values remained unaltered. Besides, the liver was partially affected, which could not represent significant changes in serum biochemistry values. Treatment of disseminated HS is still controversial; patients presenting nodules in regions that are difficult to remove or metastasis have unfavorable prognoses. Even when undergoing chemotherapy, these patients often do not exceed a survival time of more than five months (11), as observed in this case. As a support therapy, phenobarbital (2.5 mg/kg/BID) for seizure control, omeprazole (1 mg/kg/SID) for protection of gastric mucosa, and firocoxib (5 mg/kg/SID) for pain and inflammation control, were prescribed.

In the disseminated form of HS, the main affected organs are the spleen, liver, bone marrow, lymph nodes, lungs, and skin (2). Necropsy findings demonstrated lesions in almost all of these sites, including the meninges. Primary HS of the central nervous system rarely involve extracranial metastases (8), which would suggest that the neoplasia was primarily originated from the loans and the intracranial nodule was metastatic. Ocular involvement occurs in most cases, and Labrador Retrievers are commonly affected; it is usually unilateral and may be related to uveitis and blindness (9), as observed in this case.

In the present study, the findings of the cytopathological examination differed from those on histopathology; pulmonary HS may be misinterpreted as large cell anaplastic carcinoma when there is no distinction between the cell lines by immunohistochemistry. Thus, cytopathological examination for this type of neoplasia should be followed by histopathology and immunohistochemistry for confirmation (7). It was demonstrated that HS could be easily misinterpreted as carcinoma and metastatic melanoma due to the morphological similarities between these neoplasms (3). Histiocytic tumors should also be differentiated from lymphoma, poorly differentiated mast cell tumor and malignant fibrous histiocytoma, requiring immunostaining for CD antigens (4). Histopathological findings such as abundant eosinophilic, vacuolated cytoplasm and giant cells are frequently reported (3, 8), as observed in the present study.

Immunohistochemical analysis for HS should include markers CD1a, MHC class II and CD11c/CD18, which are normally expressed by interstitial dendritic cells (7). It was performed for CD3, CD20, CD18, and MHC II because it is important to rule out lymphoid origin; since HS may be misinterpreted as anaplastic large cell lymphoma, markers for B and T cell lymphoma (CD20 and CD3, respectively) were also included. The neoplastic cells were negative for these markers; however, they were strongly marked for CD18 and MHC class II, which were essential to diagnose HS (3, 8).

Considering its high-grade malignancy, animals diagnosed with disseminated HS normally show poor outcome. Complementary examinations such as imaging, cytopathology, histopathology and immunohistochemistry provide greater accuracy in the differentiation of histiocytic diseases, allowing establishing an accurate prognosis and appropriate therapies while prioritizing the maintenance of the patient's quality of life.

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