



Case Report

Malignant histiocytosis in a cat – Case report

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Abstract

A crossbred 14-year-old castrated male cat had a history of lethargy, anorexia and weight loss of one month evolution. On clinical examination, anemia, emaciation, jaundice and a large mass in the abdomen were detected. Ultrasonography revealed hepatomegaly and a single splenic mass. The cat was submitted to biopsy and euthanatized during the surgical procedure. The diagnosis of malignant histiocytosis was achieved on the basis of the clinical presentation, histopathologic and immunoistochemical findings.

Key Words: Malignant histiocytosis, histiocytic diseases, neoplasia, pathology, diseases of cats

Introduction

Histiocytic neoplasms are a group of diseases classified accordingly to local and biological behavior. Focal and self-limiting lesions (cutaneous histiocytoma), local aggressive lesions (localized histiocytic sarcoma) or multisystemic (disseminated histiocytic sarcoma) are the three major forms of the disease. Malignant histiocytosis (termed MH) is used for the disseminated form of histiocytic sarcoma (1,2,7,10). It is the most aggressive syndrome of all histiocytic neoplasms, with the most unclear origin (4). The disease is characterized by progressive and invasive multisystemic neoplastic proliferation of morphologically atypical histiocytes and their precursors (6,7) and is reported in human beings, dogs, horses and cats (4,6,7).

In dogs, several reports describe breed predisposition in Bernese Mountain dogs. MH is seen in Rottweilers and flat-coated hair retrievers, suggesting an inherited condition (4,9,13). MH is an uncommon neoplasm of cats with only a few reports of this condition

in the literature (8); It affects individuals of several ages, with no sex or breed predisposition. The most affected organs are the spleen, liver, lung and bone marrow. Cats with MH are anorexic, emaciated, lethargic, with fever and dyspnea in a few cases. Marked lymphadenopathy, hepatomegaly, splenomegaly, anemia and jaundice are the most important clinical findings reported in this species (6,11).

Case report

A 14-year-old, male, crossbreed cat was presented to the Veterinary Hospital of the Federal University of Santa Maria (HV-UFSM) with clinical signs of lethargy, anorexia, emaciation and sporadic vomiting. On clinical examination, the animal had poor nutritional status, jaundice and a large palpable mass in the abdomen. Ultrasonography revealed hepatomegaly and a single splenic tumor. Laboratory results indicated regenerative anemia (erythrocyte count: $2.97 \times 10^6/\text{mm}^3$; hemoglobin: 6.2 g/dl; hematocrit: 20% and 52 metarrubricytes/100

leukocytes); hypoproteinemia (2.6 g/dl) and icteric plasma. The cat was submitted to esophagotomy, splenectomy and hepatic biopsy. During the procedure, the cat was submitted to euthanasia due to the poor condition of the patient, presence of multiple nodules in various organs and a marked abdominal effusion.

At necropsy, the cat was icteric and with gelatinous atrophy of the subcutaneous fat. Hemothorax and hemoperitoneum were observed. Multiple elevated white nodules of different sizes (the largest with 3 cm in diameter) were observed in the cut surface of the spleen (Fig. 1a). Masses with similar characteristics were found in the lung, left lateral lobe of the liver (Fig. 1b) and in the corticomedullary region of the left kidney. Hepatic, renal and mediastinal lymph nodes were enlarged. On the cut surface, they were yellow-white and rubbery.

Tissue samples were collected, fixed in 10% formalin, routinely processed and stained with hematoxylin and eosin. Microscopically, the liver nodules were composed by sheets of histiocytic cells with abundant eosinophilic cytoplasm. The nuclei were predominantly oval and with different patterns of chromatin distribution. Few multinucleated giant cells were observed scattered in the mass (Fig. 1c). There were multiple areas of necrosis surrounded by a lymphocytic inflammatory infiltrate. Neoplastic histiocytes were also observed in the spleen although they were more diffusely arranged with obliteration of the splenic structure. Erythrophagocytosis and leucophagocytosis by neoplastic cells were frequently seen in spleen and lymph nodes (Fig. 1d). Prussian blue staining revealed large amounts of iron in the neoplastic histiocytes (Fig. 1e). The alveolar spaces of the lung were obliterated by the neoplastic cells. A large area of necrosis and arterial thrombosis were observed. In the lymph nodes, several binucleated and multinucleated cells were encountered. In the kidney, a well-defined tumor nodule composed by a population of eosinophilic, granular and foamy spindle cells were seen (Fig. 1f). In all tissues examined, bizarre mitosis were rare.

The immunohistochemical staining was performed in samples of lung and spleen using the streptavidin-biotin-peroxidase method. Briefly, 3 μ m histologic sections were pretreated for antigenic retrieval using microwave oven and TRIS-EDTA solution (pH 9,0) for 10 minutes. The slides were incubated with anti-vimentin (DakoCytomation, diluted 1:100) and anti-lysozyme (DakoCytomation, diluted 1:1000) antibodies for one hour. After incubation with the secondary biotinilated antibody, the slides were stained with DAB (DakoCytomation) and counterstained with Harris' hematoxylin. The neoplastic cells in the lung and spleen were positively stained for vimentin (Fig. 1g) and lysozyme (Fig. 1h).

Discussion

MH in domestic animals is a multisystemic neoplasm that proliferates primarily in the spleen, lungs or bone marrow. Secondary sites of neoplastic proliferation include lymph nodes and liver, with several other organs affected subsequently (8,12). Nonetheless, in most cases the primary site of origin cannot be determined.

Animals with MH have non-specific clinical manifestations. Inappetence, lethargy and weight loss are frequently seen. In cats, hyperthermia and dyspnea can be a more consistent clinical finding when there is lung involvement (9). Other clinical findings include: hepatomegaly, splenomegaly and anemia. Additional findings such as hipoproteinemia, hyperglycemia, hyperbilirubinemia, high levels of hepatic enzymes and coagulative disorders can also be found (5).

The definitive diagnosis of MH is made by histopathological examination. A widespread proliferation of anaplastic histiocytes in multiple organs, as observed in the present case, are frequently seen (8,9). Immunohistochemical markers can be used to differentiate this neoplasm from lymphoid neoplasms. However, immunohistochemistry is not always a reliable tool (3,6). In humans, positive staining for vimentin is used to differentiate MH from carcinomas and positive lysozyme immunostaining indicates a mononuclear phagocyte origin (9,11,12). In dogs, CD1, CD11b, CD11c, CD14, CD68 and MHC class II are more reliable immunohistochemical markers for cells of the histiocytic lineage. In cats, it has not yet been fully detailed the immunohistochemical profile for histiocytic neoplasms, and most of these immunological markers are not suitable for the use in formalin fixed tissues (9). In paraffin embedded formalin fixed tissues, negative staining for CD3, CD79a and CD18, associated with the morphological characteristics, can differentiate monocytic from lymphoid neoplasms (10). In this report, the positive immunostaining for vimentin and lysozyme in the neoplastic cells supports the diagnosis.

Differential diagnosis for MH should include all other histiocytic diseases, such as systemic histiocytosis, monocytic leukemia and the histiocytic form of lymphoma (3). MH can be differentiated from other histiocytic diseases for presenting high levels of cellular atypia. In systemic histiocytosis, more differentiated histiocytes display a marked predilection for the skin and peripheral lymph nodes (2,3,14). Multinucleated cells, erythrophagocytosis and leucophagocytosis are the hallmarks of histiocytic sarcomas. This feature is believed to be responsible for the anemia in the present case (7, 8, 9). MH is a diagnosis of exclusion and can be done when the tumor cells have morphological, immunohistochemical (9) and ultrastructural characteristics with those of histiocytes (3).

Treatment for MH is based on chemotherapy protocols for lymphoma. However, satisfactory results have not been achieved. The prognosis of the disease in cats appears to be more obscure than in dogs. Several

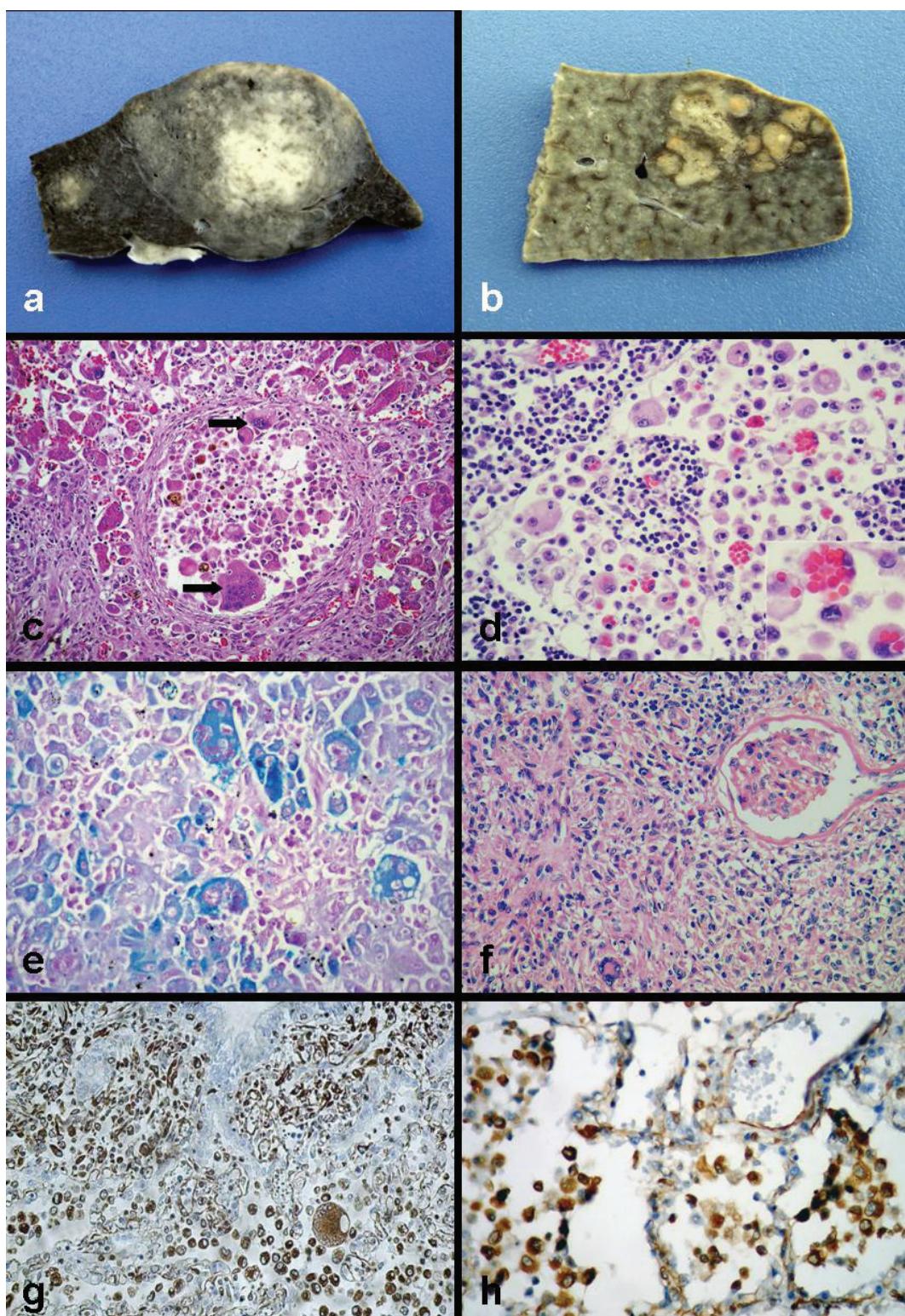


Fig. 1a – Spleen. An elevated white nodule was observed on the cutting surface. **Fig. 1b** – Liver, left lateral lobe. Multiple irregular nodules invade the parenchyma. **Fig. 1c** – Liver. Micrography of a neoplastic nodule where multinucleated giant cells are seen (arrows). H&E, Obj 40. **Fig. 1d** – Lymph node. Several binucleated and multinucleated cells were encountered. Inset: Erythrophagocytosis was frequently found. H&E, Obj. 40. **Fig. 1e** – Spleen. Large amounts of iron are observed within the cytoplasm of the neoplastic histiocytes. Prussian blue, Obj. 40. **Fig. 1f** – Kidney. Neoplastic proliferation composed of a population of eosinophilic and granular spindle cells. H&E, Obj. 20. **Fig. 1g** – Lung. Neoplastic cells are strongly marked for vimentin. Streptavidin-biotin-peroxidase method. Obj. 20. **Fig. 1h** – Lung. Expression of lysozyme by the neoplastic histiocytes. streptavidin-biotin-peroxidase method. Obj. 40.

reports correlate the disease in cats with poor prognosis and death in a short period of time (9).

Considering that data on prevalence, average age of incidence as well as gross and histologic changes of this tumor are scant, we found important to describe this condition and suggest to small animal clinicians to make an early diagnosis to differentiate this poor prognosis condition from other treatable diseases of cats.

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