

A case of canine malignant histiocytoma

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Abstract

A 13 year-old mixed-breed male dog was presented for a second opinion at the veterinary clinic with a tumor of approximately 15 cm³ on its abdomen. Fine-needle aspiration and cytological examination revealed moderately and distinctly dysplastic mesenchymal cells. Abdominal radiographs showed the extent of the tumor, which had developed mostly inside the abdomen. Radiography and CT revealed possible metastasis to the lungs. A diagnosis of malignant histiocytoma was made. The tumor was surgically removed at the owner's request, but the dog died 5 days later. We follow with a case discussion, as well as the treatment and prognosis for this type of tumor.

Keywords: malignant histiocytoma, dog, abdominal radiographs, metastasis, histiocytic sarcoma

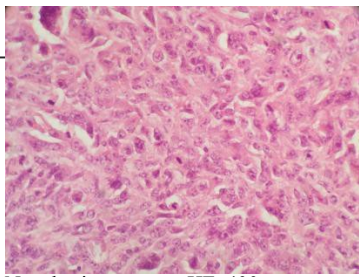
Introduction

The histiocytic sarcoma complex (HSC) is a group of neoplasms characterised by the proliferation of dendritic cells of either Langerhans cell or interstitial dendritic cells lineage that affects both dogs and cats, although the disease is more infrequent in cats (Klopfleisch R, 2016; Moore et al., 2006). Dog breeds more commonly affected by HS are the Bernese Mountain Dog, Flat-Coated Retriever, Rottweiler, Golden Retriever and perhaps miniature schnauzer (North S, Banks T, 2007; Lenz JA et al, 2017; Abadie et al, 2009). The HSC manifests under three forms: as localised lesions of single organs, as disseminated lesions in multiple organs or as hemophagocytic histiocytic sarcoma (HHC), a particular form arising from splenic macrophages (Withrow SJ et al., 2013; Moore PF, 2014).

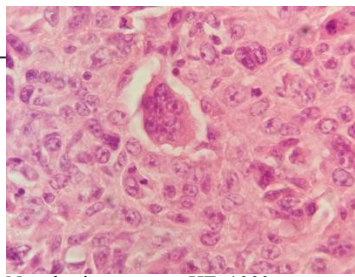
The first form, called histiocytic sarcoma, is usually localised in the spleen, lymph nodes, lung, bone marrow, skin and subcutis, brain or the articular tissue of appendicular joints (Moore PF, 2014). It is composed of highly pleomorphic round cells, varying in cell and nucleus size and ratio (Withrow SJ et al., 2013).

The second form, formerly designated as malignant histiocytoma (currently disseminated HS) occurs as more than one lesion in a single organ that rapidly spread to other locations (Moore PF, 2014). It has a more heterogenous appearance, comprising round, oval and spindle-shaped cells that are less pleomorphic but present more morphological features of malignancy (Withrow SJ et al., 2013; Moore PF, 2014). Other authors describe the disseminated form as the progression of the localised form beyond the regional lymph nodes, commonly to the lung, spleen, and lymph nodes (Klopfleisch R, 2016).

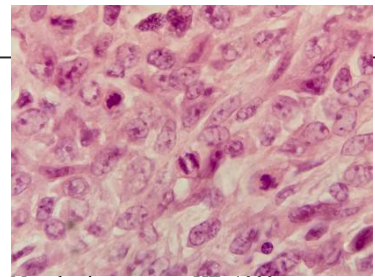
The third form, hemophagocytic histiocytic sarcoma, is the most distinctive; it derives from splenic macrophages and localises in the spleen, liver, bone marrow, and lung (Klopfleisch R, 2016). The cells are hard to differentiate from macrophages found in inflammatory lesions, as they can present little to no malignancy features and it clinically manifests as a hemolytic anemia that does not respond to the use of immunosuppressives (Withrow SJ et al., 2013; Moore PF, 2014).



Neoplastic structure, HE, 400x - Abundant neoplastic cells with marked pleomorphism. Source: prepared by the authors



Neoplastic structure, HE, 1000x - Mesenchymal cells with a malignant morphology - multinucleated cancer cells. Source: prepared by the authors.



Neoplastic structure, HE, 1000x - Mesenchymal neoplastic cells: marked anisokaryosis, euchromatic nuclei, evidently nucleolated nuclei, atypical mitoses. Source: prepared by the authors.

Figures 1-3. Histologic aspects of Gimmi's histiocytic sarcoma. Source: prepared by dr. Teodoru Soare.

Localised and disseminated HS present as white masses with a smooth cut surface, but they can also present red mottling (due to hemorrhage and necrosis), usually with distinct and unencapsulated margins, and differentiate from the hemophagocytic variant, which appears as a diffuse infiltrate in the affected organs (Meuten DJ, 2016; Klopffleisch R, 2016).

Clinical signs depend on the affected organ(s), but are generally non-specific (anorexia, lethargy, malaise, weight loss) (Klopffleisch R, 2016). The mass effect of internal tumors can generate signs from unaffected organs (Klopffleisch R, 2016). Paraclinic findings might include a mild anemia (HS, diffuse HS) or a severe anemia (HHC), thrombocytopenia, hypoalbuminemia and rarely neutrophilia, hypercalcemia or hyper-gammaglobulinemia (Klopffleisch R, 2016, Argyle DJ et al, 2008). As hyperferritinemia seems to be common in dogs with HS, ferritin may be a useful serum biomarker for this neoplasm (Friedrichs et al, 2010).

Treatment options are wide surgical excision and chemotherapy (Meuten DJ, 2016, Klopffleisch R, 2016). The localised form is curable with surgery, if the lesion is detected early; once the disease spreads the treatment is palliative chemotherapy (Meuten DJ, 2016). Chemotherapy for disseminated HS with lomustine, an alkylating agent, at 60–90 mg/m² may prolong survival times in responsive dogs (Klopffleisch R, 2016; Skorupski KA et al, 2007; North S and Banks T, 2007). Epirubicin, dacarbazine and other substances can be used in dogs that do not respond to lomustine with variable results (Mason SL, 2017; Kezen KA, 2017, Moore AS, 2017). The prognosis is poor for all forms except localised HS (Klopffleisch R, 2016, Meuten DJ, 2016; Dervisis NG, 2016; Moore AS, 2017).

There is a report on the successful treatment of 4 cases of canine disseminated HS with the human major histocompatibility complex nonrestricted cytotoxic T-cell line TALL-1041 (Vissonneau S et al, 1997), but this is option is not currently widely available.

Materials and Methods

Complete blood counts were performed in-house using a Mindray BC-2800 Vet automatic hematology analyzer. Blood biochemistry was performed in-house using a Rayto RT-1904C semiautomatic chemistry analyzer. Cytology and histopathology were performed Dr. Teodoru Soare at the Faculty of Veterinary Medicine Bucharest. The radiologic and CT examinations were performed by dr. Florin Grosu at 4VET Radiology Center. The ultrasonographic examinations were performed with a portable color Doppler Sonoscape S2 system by dr. Otilia Cristea and dr. Radu Constantinescu.

Case Presentation

A 13 year-old medium-sized mixed-breed male dog was presented for a second opinion at the veterinary clinic for a large tumor on it abdomen (figure 4). The dog had been neutered at the age of 2. The tumor was extremely large (approximately 15 cm³) and had already invaded the abdomen, making the point of origin impossible to discern. Ghimi manifested an intermittent fever, having evening episodes of pyrexia with a body temperature oscillating between 40-42°C, registering an optimal temperature during the day). The dog also presented with vomit during the febrile periods and a loose stool the next morning. Ghimi had inspiratory dyspnea, in his attempt to compensate with prolonged, deep inspirations. The body condition score was 2/5 (AAHA Body Condition Scoring Systems, 2010).



Figure 4. Preoperative aspect of the tumor. Source: from the authors.

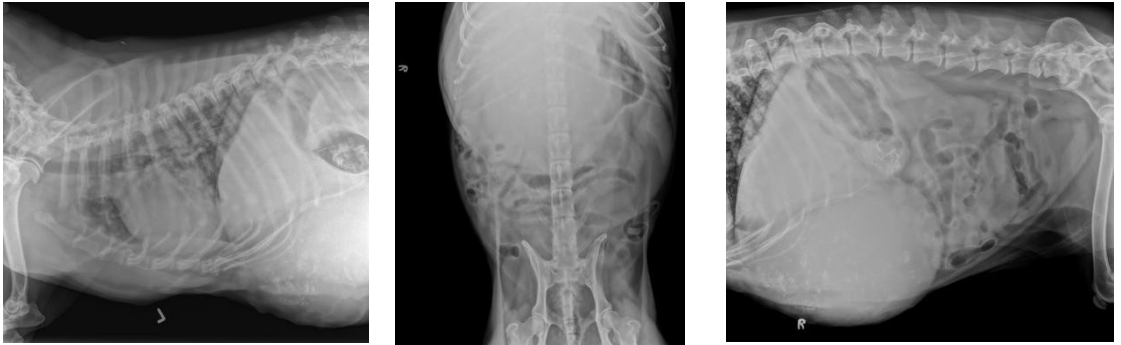
Palpation of the abdomen was impossible due to the extent of the growth. The superficial lymph nodes (popliteal, axillary and prescapular) were reactive; the reactivity of the submandibular lymph nodes could have also been due to the presence of advanced periodontal disease and infection. At this point, the dog was not eating and received supportive treatment (iv fluids, aminoacids), iv broad-spectrum antibiotics (ceftriaxone), pain medication (tramadol) and corticosteroids.

A CBC revealed a leukemoid reaction, as a physiological response to stress and infection (WBC 100.9 - reference values 6-17 K/ μ L), with mild lymphocytosis and intense neutrophilia, a decreased RBC count (3.64, reference 5.5-8.5 M/ μ L) and hematocrit (26.8 reference 39-56%) with increased hemoglobin (24, reference 11-19 g/dL). Blood biochemistry was unremarkable except for the alkaline phosphatase (1114.17, reference 10.6-100.7 U/L) and serum amylase (3965.84, reference 269.5-1462.4 U/L). By the second day of ceftriaxone and hydrocortisone hemisuccinate the dog improved, with the disappearance of the digestive signs and the improvement of the respiratory effort. Ultrasound identified a soft tissue mass of variable echogenicity due to areas of necrosis and mineralization.

Two ultrasound guided fine needle aspirates were evaluated cytologically, but due to the presence of inflammatory cells and necrotic debris, they were deemed inconclusive. They did, however, reveal a few moderately and distinctly displastic mesenchymal cells alongside red blood cells, neutrophils, macrophages and lymphocytes. A decision was taken to further investigate the patient in order to establish a conclusive diagnostic.

In order to evaluate the extent of the tumor and to identify the presence of any metastases, Ghimi was referred for thoracic and abdominal radiography. The radiographs revealed disseminated nodular densifications in the lung (figure 5) and the magnitude of the abdominal

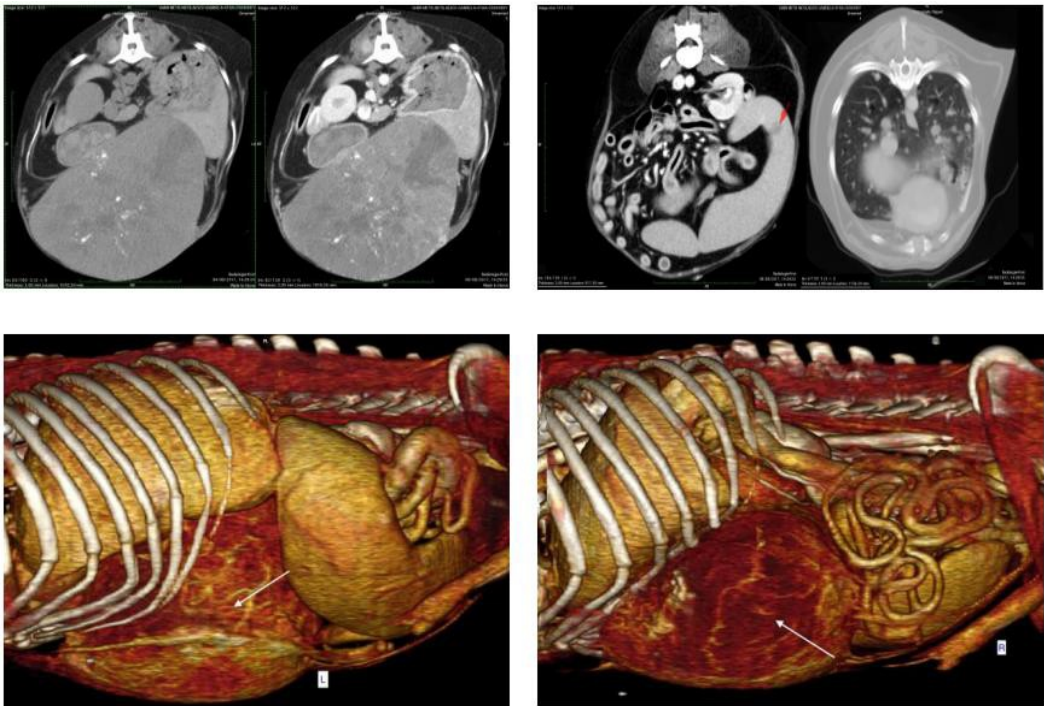
tumor, which displaced the stomach, lung and intestines. The radiologic appearance of the tumor was of a macronodular densification of soft tissue with areas of amorphous calcification at the right thoraco-abdominal junction of approximately 14 cm/19 cm (figures 6-7).



Figures 5-7. Ghimi's thoracic (left) and abdominal (center, right) radiographs. Note the presence of nodular lesions in the lung, probably lung metastases and the gross displacement of the organs in the abdominal cavity.

Images courtesy of dr. Grosu Florin, 4Vet Radiology Center, Bucharest

At the owner's insistence that the animal be operated and the tumor removed the dog was again referred for computerized tomography. The surgeon agreed to palliative surgery to remove the large abdominal tumor and improve comfort.



Figures 7-12. Top: CT images of the tumor, spleen and lungs. Bottom: 3D reconstruction of the tumor and surrounding organs. Images courtesy of dr. Grosu Florin, 4Vet Radiology Center, Bucharest.

The CT examination described a heterogenous soft-tissue tumor (figures 7-8, 11-12) located in the cranial and ventral mid-abdomen, with relatively well delineated margins of approximately 20 cm*13 cm*18 cm (L*H*D). The growth has a significant mass effect over the surrounding organs (spleen, liver, gallbladder, small intestine and colon. Its heterogenicity was due to hypoattenuation probably caused by areas of hemorrhagic fluid or necrosis, but also to areas of mineralization/calcification. The tumor filled moderately and irregularly with contrast, which permitted the identification of the tumor's origin to the right ventro-lateral abdominal wall. Its growth had remodelled the orientation of the floating ribs, whose distal half became horizontal. Both lungs presented micro and macro interstitial nodules (figure 10). On the head of the spleen there was a hypoacoustic area of 1.5-2 cm in diameter (figure 9) that did not fill up with contrast (another possible metastasis).

Before the surgery, blood biochemistry revealed an improvement in serum biochemical parameters: serum amylase decreased to half of its initial value and alkaline phosphatase decreased slightly, with the exception of urea, which doubled to 75.75 mg/dL (reference 8.8-25.9 mg/dL). CBC showed continous lymphocytosis (to half the initial value), an increased RBC count and hematocrit with decreased hemoglobin.

According to the owner's wishes, the team proceeded with the surgical excision, despite being warned of the grave prognosis and the small chances of long-term survival. The tumor was removed successfully (figures 12-15), but the dog evolved well for two days but on day three he decompensated (respiratory and circulatory decompensation) and died five days avter the intervention. A histopathologic analysis confirmed the suspicion of histiocytic sarcoma.



Figures 10-13. Intraoperative aspects. Source: from the authors.

Conclusions

Due to the extent of the disease, in Ghimi's case treatment was illusory. Currently, HS is only curable before it metastasises through wide surgical excision. But for the owner's insistence for sugery, the correct approach would have been to treat with palliative chemotherapy. A tumor this size and with such a compressive effect was not well suited for palliative surgery, as the dog decompensated and subsequently died. We recommend that any growth should be investigated as soon as it is detected and ideally, yearly check-ups should include abdominal ultrasonography.

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