Primary Gastric Histiocytic Sarcoma in a Dog – A Case Report

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Summary

A 12-year-old intact female mixed breed dog was presented for chronic, intermittent vomiting and diarrhoea. On endoscopic examination a protruding mass arising from the mucosal surface of the pyloric region was detected. Cytological and histological examination revealed an accumulation of pleomorphic round/oval phagocytic cells suggesting histiocytic origin. This was confirmed by immunohistochemistry. No extra-gastric involvement was detected on clinical examination or at necropsy. This is the first report of primary gastric histiocytic sarcoma in a dog.

Introduction

Tumours of the glandular stomach in domestic animals are not common. In carnivores gastric neoplasia accounts for < 1% of all malignancies (Guilford and Strombeck, 1996). Primary gastric neoplasms mostly affect older dogs; carcinomas (of all histological types) are the most frequently reported primary tumours followed by smooth muscle tumours (leiomyomas and leiomyosarcomas). Male dogs are more commonly affected (Guilford and Strombeck, 1996; Head et al., 2002). Benign epithelial tumours are much less common and are often described as incidental lesions at necropsy, appearing as solitary, polypoid masses in the pyloric region. According to a WHO survey, lymphoid tumours are common, but may not be primary gastric tumours (Head et al., 2002). Among lymphoid neoplasms, a case of canine gastric extramedullary plasmacytoma has been described (Brunnert et al., 1992). Only two cases of canine gastric carcinoids have been reported (Albers et al., 1998; Head et al., 2002). Secondary tumours are rare: metastatic carcinoma and mesothelioma are reported in domestic animals (Head et al., 2002). Rare cases of canine malignant histiocytosis with secondary gastric involvement have also been reported (Moore and Rosin, 1986; Rosin et al., 1986; Hayden et al., 1993; Ramsey et al., 1996; Affolter and Moore, 2002).

The aim of this paper is to discuss the clinical presentation as well as the histological and immunophenotypic characteristics of a canine HS localized to the gastric mucosa and submucosa.

Case History

A 12-year-old female mixed breed dog was presented to the ‘San Marco’ Veterinary Clinic of Padua (Italy) in poor condition. The owners reported chronic vomiting recently associated with bloody vomiting and diarrhoea. The dog had been empirically treated with cimetidine and metoclopramide for 4 months with negligible results.

Clinical Findings

On physical examination the dog was emaciated and had abdominal pain. A complete blood count revealed moderate and regenerative anaemia, severe leucocytosis with left shift and monocytosis. Platelet estimation and count were inadequate. The serum chemistry profile indicated hypoprotidemia and increased urea as signs of ongoing gastrointestinal bleeding (Table 1).

By means of ultrasonographic, tomographic and endoscopic examination, a gastric mass was observed (Fig. 1). On endoscopic examination, the gastric body was unremarkable with only the presence of a small amount of yellow–brown fluid in the gastric lumen. A large, protruding and ulcerated mass was observed in the distal pyloric antrum; the pyloric orifice was occluded in this view. The surrounding mucosa was reddened and irregularly thickened. A total of 12 biopsy samples from both the mass and surrounding tissue were obtained: sampling was performed several times in the same location in an effort to obtain an adequate tissue sample. No abnormalities were found during endoscopic inspection of the proximal and distal descending duodenum; several biopsies were obtained from different duodenal areas. Ultrasonographic and tomographic examination revealed no abnormalities in the thoracic or in the other abdominal organs.

Pathological Findings

Three biopsies from the pyloric mass were prepared by squash technique to obtain cytological samples which were air-dried...
and stained with May-Grunwald–Giemsa stain in an automatic slide stainer (7100 Aerospray®/C210 Slide Stainer; Wescor, Logan, UT, USA). Cytological samples were highly cellular, showing several clusters of superficial epithelial cells of the gastric mucosa with a regular honeycomb architecture. Many atypical large cells with prominent anisocytosis and anisokaryosis were observed scattered throughout mildly dysplastic epithelial clusters; the N : C ratio was variable but often high and nuclei had an irregular shape with coarse chromatin and multiple prominent nucleoli. Multinucleated, markedly atypical cells were also occasionally observed showing erythrophagocytosis (Fig. 3a).

Remaining biopsies were fixed in 10% buffered formalin, embedded in paraffin, sectioned at 5 μm and stained with haematoxylin and eosin (H&E). Histological examination revealed dense infiltration of the superficial lamina propria propria mucosae by round to polygonal, variably sized atypical cells with abundant eosinophilic cytoplasm. Multinucleated giant cells were observed. Foci of small lymphocytes as well as superficial areas of neutrophilic infiltration were also observed. Duodenal biopsies revealed moderate lympho-plasmacytic inflammation.

Table 1. Haematological and serum biochemical values

<table>
<thead>
<tr>
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<th>Values</th>
<th>Reference range</th>
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<tr>
<td><strong>RBC (∗10^{12}/l)</strong></td>
<td>3.89</td>
<td>5.70–8.80</td>
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<tr>
<td><strong>Haematocrit (%)</strong></td>
<td>27.5</td>
<td>37.1–57.0</td>
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<tr>
<td><strong>Haemoglobin (g/l)</strong></td>
<td>91</td>
<td>129–184</td>
</tr>
<tr>
<td><strong>Reticulocytes (%)</strong></td>
<td>4.9</td>
<td>0.1–2.0</td>
</tr>
<tr>
<td><strong>Reticulocytes (∗10^9/l)</strong></td>
<td>190.610</td>
<td>8.400–129.300</td>
</tr>
<tr>
<td><strong>WBC (∗10^{9}/l)</strong></td>
<td>74.94</td>
<td>5.20–13.90</td>
</tr>
<tr>
<td><strong>Lymphocytes (∗10^9/l)</strong></td>
<td>3.747</td>
<td>1.300–4.100</td>
</tr>
<tr>
<td><strong>Monocytes (∗10^9/l)</strong></td>
<td>7.494</td>
<td>0.200–1.100</td>
</tr>
<tr>
<td><strong>Band neutrophils (∗10^9/l)</strong></td>
<td>3.747</td>
<td>0–0.300</td>
</tr>
<tr>
<td><strong>Segmented neutrophils (∗10^9/l)</strong></td>
<td>59.952</td>
<td>3.900–8.000</td>
</tr>
<tr>
<td><strong>Eosinophils (∗10^9/l)</strong></td>
<td>0</td>
<td>0–0.600</td>
</tr>
<tr>
<td><strong>Basophils (∗10^9/l)</strong></td>
<td>0</td>
<td>0–0.100</td>
</tr>
<tr>
<td><strong>Platelets (∗10^9/l)</strong></td>
<td>24</td>
<td>143–400</td>
</tr>
<tr>
<td><strong>Total protein (g/l)</strong></td>
<td>55</td>
<td>57–77</td>
</tr>
<tr>
<td><strong>Urea (mmol/l)</strong></td>
<td>23.205</td>
<td>5.355–16.065</td>
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RBC, red blood cells; WBC, white blood cells.
distinct granular pattern for the former (Fig. 5a) and a diffuse pattern for the latter (Fig. 5b). Some small, differentiated macrophages were positive for MAC387.

Discussion
The diagnosis of histiocytic neoplasia based on cytological and histological examination was confirmed by immunohistochemistry. Tumour cells had histiocytic features such as phagocytic activity, and their immunophenotype indicated histiocytic origin (i.e. cytoplasmic labelling by lysozyme and vimentin, and absence of reaction for lymphoid and other mesenchymal markers) according to previous studies (Moore, 1986; Moore and Rosin, 1986; Hayden et al., 1993; Brown et al., 1994; Carioto, 1997; Chandra and Ginn, 1999; Uchida et al., 2001). Features of malignancy were marked cellular pleomorphism and the presence of atypical mitosis. Because the lesion was solitary, it was diagnosed as localized HS.
On histological examination of H&E stained sections, the diagnoses of anaplastic carcinoma, poorly differentiated mesenchymal tumour, and lymphoid neoplasia with atypical plasma cell features were also considered. Suspicion of epithelial origin was prompted by the observation of atypical cells with eccentric, crescent-shaped nuclei conferring a 'signet-ring' like morphology, as observed in some gastric carcinomas (Head et al., 2002); lymphoid origin was considered because of some cytological similarities with polymorphous blastic type canine extramedullary plasmacytoma (Platz et al., 1999). All these hypotheses were eliminated because of immunohistochemical results that were negative for cytokeratin, actin, desmin, S100, CD117, CD3 and CD79.

In domestic animals, histiocytic proliferative diseases have come under intense scrutiny in recent years (Affolter and Moore, 2002). Histiocytic malignancies are distinguished based upon their distribution (localized and disseminated HS) and with respect to tumour cell origin. They can be functionally divided into dendritic cell (DC) tumours and macrophage tumours, the latter displaying prominent haemophagocytosis (Moore, 2002). Histiocytes are a heterogeneous group of cells with different morphological and functional features. The macrophages (or phagocytes) are involved with inflammatory processes, have high lysosomal enzyme content (lysozyme and α1-antitrypsin) and are capable of varying degrees of phagocytic activity. The DC compartment comprises: (i) the follicular DC of the germinal centre of lymph nodes, (ii) the Langerhans cell (LC) of the skin, epidermis, cervix, vagina, stomach and oesophagus, (iii) the interstitial DC representing the counterpart of LC in parenchymal organs (with the exclusion of brain and cornea), (iv) the veiled cell (indeterminate cell), derived from LC or interstitial DC and migrating to local lymphoid tissue following antigen capture, and (v) the interdigitating DC of the T-zone of lymph nodes. All of these cells typically have dendritic morphology and low levels of lysosomal enzymes, are mostly incapable of phagocytic activity and play a key role in antigen presentation to lymphocytes. The different types of DC can be distinguished by a combination of morphologic and immunophenotypic characterization (Pileri et al., 2002). The development of appropriate immunophenotyping reagents for the dog permits the distinction between benign and malignant histiocytic diseases such as cutaneous histiocytoma (a benign epitheliotropic proliferation of epidermal LC), reactive histiocytosis (a non-neoplastic cutaneous or systemic immunoregulatory disorder) and localized or disseminated HS (Moore, 2002).

Histiocytic sarcoma was first described in the Bernese mountain dog and subsequently in other breeds. Localized HS develops from a single site (generally in the subcutis), is locally invasive, metastasises to draining lymph nodes and generally appears less devastating than its disseminated counterpart, which affects predominantly internal organs (Affolter and Moore, 2002). In a recent compilation dealing with 19 localized and 20 disseminated canine HS of DC origin, epidemiological analysis revealed a high frequency in Rottweilers, Bernese mountain dogs and Golden Retrievers (five, three and three of 19 patients with localized HS and six, five and two of 20 patients with disseminated HS, respectively). Clinical and histopathological examination revealed that 13 of the 19 localized HS were in the subcutis and in the skeletal muscle; all except one were found on the limbs and the remaining one in the chest. The other six cases affected the spleen (with multiple hepatic metastases), tongue, lung, brain stem, nasal cavity,
vertebral bone and epidural space. Metastases in lymph nodes were present in three cases. Disseminated HS were most often found in the spleen (16 of 20 cases), peripheral lymph nodes (12/20), liver and bone marrow (11/20 for each location), lung (10/20), subcutis and submucosal muscle (seven of 20), kidney (six of 20). Less frequent were metastases to the heart (two of 20), oral and nasal cavity, brain, prostate, adrenal glands and testicles (one case per organ) (Affolter and Moore, 2002). Other unusual tumor locations of HS reported in the literature are: pancreas, joint capsule, meninges, pituitary, gingiva, pleura and digestive tube (Hayden et al., 1993; Brown et al., 1994; Carioto, 1997; Chandra and Ginn, 1999; Uchida et al., 2001; Pool and Thompson, 2002). Gastric involvement was reported by Moore and Rosin (1986) and by Rosin et al. (1986) in single cases of disseminated HS with multicentric visceral and cutaneous infiltrates. It remains unknown whether disseminated HS arises as a primary multicentric malignancy; alternatively, it may represent a terminal stage of a localized HS of an internal organ with rapid proximal and distant spread (Affolter and Moore, 2002).

No cutaneous, thoracic or extra-gastric abdominal involvement was detected on gross examination in our study. Because no histological examination of other organs was performed, we were not completely confident in ruling out visceral spread of the tumor. Nevertheless, the lack of evidence of extra-gastric involvement on gross and clinical examination led us to suspect the existence of a primary and solitary gastric histiocytic malignancy.

Typing of histiocytic neoplasia is possible by performing immunohistochemical analyses on frozen samples. CD1, CD11b, CD11c, CD14, CD68 and MHC class II are considered the most reliable markers for identifying histiocytic origin and differentiating between DC origin (CD1 + and CD11c+) and macrophage origin (CD11b+, CD14+ and CD68+) (Moore, 2002). The majority of macrophages in several tissues, such as lymph node, spleen, pulmonary alveoli and lamina propria of the gut, are known to contain abundant lysozyme; in contrast, dendritic antigen-presenting cells lack appreciable lysozyme (Moore, 1986). Our immunohistochemical results on a formalin-fixed, paraffin-embedded sample were suggestive of macrophage origin: staining for lysozyme resulted in granular labelling of the cytoplasm of a large number of neoplastic cells. Evidence of phagocytosis also suggests that the tumour cells are of macrophage origin.

To our knowledge, this is the first report dealing with a suspected primary localized HS in the gastric mucosa and submucosa in the dog. Furthermore, HS of macrophage origin appears to be unusual in dog. In the large series of cases of localized and disseminated canine HS studied by Affolter and Moore (2002), the dendritic immunophenotype (determined on frozen samples) was observed in all cases.

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References


