SIGNET-RING CELL GASTRIC CARCINOMA IN A DOG


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SUMMARY

Owing to its rarity, the clinical sign of chronic vomiting is usually diagnosed as foreign body obstruction or as an intestinal accident. Unfortunately, gastric carcinoma is usually never considered as a differential in such cases. This paper describes the pathology of signet-ring cell gastric carcinoma in a dog that had a history of chronic vomiting and haematemesis along with associated haemogram and clinical biochemical changes pertaining to this tumour.

Keywords: chronic vomiting, haematemesis, signet-ring cell gastric carcinoma

INTRODUCTION

Although rare in domestic animals, the prevalence of gastric carcinoma is highest in dogs (Withrow, 1996). The stenotic effect of this carcinoma on the stomach is known to lead to vomiting, abdominal pain, anaemia, weight loss, haematemesis and malaena in dogs (Fonda et al., 1989). In all cases, vomiting is the predominant sign which may appear as early as six months prior to diagnosis. This paper describes a case of gastric carcinoma in a dog with the characteristic clinical-pathological feature of this tumour.

CASE HISTORY

The dog was a 14 year-old spayed Spitz that had a history of chronic vomiting, inappetence and haematemesis for the past month. On physical examination, the dog was found to be thin, depressed and anaemic. However, no abdominal pain or masses was found. This led to differential diagnoses of gastritis, hepatic or renal insufficiency and neoplasia. Blood was taken for liver and kidney enzymes while treatment for vomiting and inappetence was advocated. Oral metoclopramide (Metoclopramide Omega®) and vitamin B complex were prescribed.

The following day, the dog was brought in again since it continued to vomit despite being given the prescribed drug. Thus, another set of treatment was prescribed with the addition of fluid therapy for 5% dehydration, tagamate (Cimetidine®) and carafate (Sulcrafate®) for gastritis/ulceration and amoxicillin (Amoxil®). As vomiting did not cease, the regime for metoclopramide was changed from oral to the intravenous route.

It was hospitalised for seven days prior to its death on 24 August 2004. During hospitalisation, blood samples were taken. Survey and contrast (Iohexol, Omnipaque®) radiography and ultrasound were performed on the abdomen.

Clinico-pathologic findings

During hospitalisation, the frequency and severity of vomiting did not subside despite the treatment. The haemogram revealed a regenerative anaemia with a left shift (Table 1) and the vomitus was confirmed to contain blood.

Table 1: Selected blood parameters of the dog following the first day of hospitalisation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Values</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (X1012/l)</td>
<td>5.5-8.5</td>
<td>3.43</td>
</tr>
<tr>
<td>Haemoglobin (g/l)</td>
<td>74</td>
<td>120-180</td>
</tr>
<tr>
<td>PCV (l/l)</td>
<td>0.35-0.55</td>
<td>0.22</td>
</tr>
<tr>
<td>Luecocytes (corrected) (X109/l)</td>
<td>6.0-17.0</td>
<td>25.9</td>
</tr>
<tr>
<td>Band neutrophils (X109/l)</td>
<td>0.0-0.3</td>
<td>2.33</td>
</tr>
<tr>
<td>Segmented neutrophils (X109/l)</td>
<td>3.0-11.5</td>
<td>24.72</td>
</tr>
<tr>
<td>Nucleated RBCs (/100WBC)</td>
<td>Rare</td>
<td>2</td>
</tr>
<tr>
<td>Reticulocytes (/100RBC)</td>
<td>0.5-1.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Plasma protein (g/l)</td>
<td>60-80</td>
<td>72</td>
</tr>
<tr>
<td>Icteric index (units)</td>
<td>2-10</td>
<td>2</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>5-90</td>
<td>25.5</td>
</tr>
<tr>
<td>BUN (mmol/l)</td>
<td>3-7.5</td>
<td>6.1</td>
</tr>
<tr>
<td>Creatinine (umol/l)</td>
<td>88-176</td>
<td>117</td>
</tr>
</tbody>
</table>

The survey X-ray revealed a lobulated liver while the contrast radiogram showed filling defect at the pyloric region. Thickening of gastric wall along with a lobulated liver was scanned on ultrasound.
Fig. 1. Photograph of the thickened and stenotic pylorus (arrow)

Fig. 2. Photograph of the mottled and shrunken lobulated liver

Fig. 3. Photomicrograph of the tumour denoting its scirrhous nature in the pylorus (H&E, X 40)

Fig. 4. Photomicrograph of the tumour in the pylorus depicting the presence of signet-ring cell (H&E, X100)

Fig. 5. Photomicrograph of the tumour in the stomach showing signet-ring cell being laden with mucin (PAS, X400)

Fig. 6. Photomicrograph of the liver showing clusters of scirrhous (arrows) appearance of the tumour cells
Post mortem findings

Grossly, there was a 4 cm thick greyish scirrhous mass encircling the pyloric mucosa (Fig. 1). This annular fold of mass was found to obliterate more than 85% of the pyloric lumen. Apart from a thickened gastric mucosa, the mottled liver was also nodular and slightly smaller (Fig. 2).

Microscopically, the scirrhous mass consisted of massive fibrous stroma along with sac-like nest of cells (Fig. 3). Although the cells were pleomorphic, the general appearance tended to show up as cuboidal cells, many of which also exhibited signet-ring forms (Fig. 4). The PAS stain performed on all tumour tissues (pylorus and liver) demonstrated that majority of the signet-ring cells were laden with mucin (Fig. 5).

Hepatocytes were in different stages of fatty degeneration, and in some areas, scirrhous arrangements of cells similar to those seen in the mass were evident (Fig. 6). Such cells were also seen to be present in blood vessels and its vicinity.

DISCUSSION

In majority of gastric carcinoma cases, vomiting is the most consistent and predominant clinical signs observed (Fonda et al., 1989). Vomiting can be seen as early as one to six months prior to the diagnosis of this tumour in dogs. In our case, the vomiting was more of haematemesis as confirmed by the presence of occult blood in the vomitus. Owing to the size of the tumour and the frequency of vomiting during hospitalisation, the dog could have been having bouts of vomiting for more than a month as stated.

The radiography and ultrasound results aided the diagnosis of this tumour. Hypoechoic transmural gastric wall thickening with altered layering as found in this dog during ultrasound examination is highly suggestive of gastric carcinoma (Beck et al., 2001). This feature is a result of the tumour arising from the submucosa and massively infiltrating the gastric musculatures (Pennick et al., 1998)

Another factor that might have easily led to the suspicion of gastric carcinoma in this dog is its age. Dogs older than three years are usually affected by gastric carcinoma (Gualtieri et al., 1999) and in our case, the age of 14 years surpassed the mark of age susceptibility to this tumour.

Likewise, the region (pylorus) where the tumour was found is also a predilection site for this tumour. It has been observed that gastric carcinoma commonly occurs at the pyloric, cardia and antral region while the fundus is a rare site. In addition, the gross annular and stenosing (Lingeman et al., 1971; Fonda et al., 1989) appearance of the tumour in the case presented here further confirms the likelihood of a gastric carcinoma.

Undoubtedly, the cellular feature (both on H&E and PAS stains) of the tumour conforms to that of a gastric carcinoma. The pronounced fibrosis, infiltration clusters of pleomorphic cells throughout all layers of the stomach as evident in this case are striking features of this tumour. Furthermore, the presence of signet-ring cells laden with mucin endorsed the definitive diagnosis of gastric carcinoma (Fonda et al., 1989).

The presence of such cells in the liver signified the aggressive nature of this tumour and can be classified as T3NOM1 based on the WHO classification (Hamilton and Aaltonen, 2000). It is also believed that degenerative changes in the liver are possibly secondary to the presence of this tumour due to the competition between tumour cells and hepatocytes for nutrient. Alternatively, compression of the vessels and sinusoids by the tumour cells could also have led to such degenerative changes.

No correlation exists between high prevalence in humans as compared to animals in this area. This could be due to animals being better at avoiding prolonged contact with carcinogens or that animals are inherently more resistant than man to the carcinogens. Thus, the rarity of this case in dogs is simply because Malaysians have a very low rate of gastric carcinoma (Kurioshi et al., 1994).

Several factors are suspected to play a role in gastric carcinogenesis, including the effects of diet, exogenous chemicals, intra-gastric synthesis of carcinogens, genetic factors, infectious agents and pathological conditions in the stomach (Stadtlander and Waterbor, 1999). Likewise, it is almost impossible to determine the exact aetiopathogenesis in the case presented owing to the prolonged onset of the signs and rather poor history.

Although a number of genetic and molecular alterations have been described (Gao et al., 2001; Tamura et al., 2001; Yokozaki et al., 2001), the pathogenesis of gastric carcinoma remains is still a state of flux. However, the mechanism by Correa (1992) postulating the initial involvement of gastritis ending in metaplasia, dysplasia, and finally gastric carcinoma is widely accepted. It is very likely that the dog in the case reported could have also been going through such pathogenetic mechanisms. This is because of slow onset or a long period of vomiting.

Finally, the alteration or loss of E-cadherin expression seems to be critical for the development of gastric carcinomas. Furthermore, abnormal E-cadherin-catenin complex expression occurred in early gastric carcinomas and changes in E-cadherin expression might be early events in gastric carcinoma (Blokk et al., 1999; Xiangming et al., 1999; Ohene et al., 2000). Abnormal expression of the E-cadherin-catenin complex occurs frequently in gastric carcinoma, and is closely related to its histogenesis (Zhou et al., 2002). In our case, no further immunohistochemical test was done since the microscopic appearance of the tumour stained by H&E and PAS were characteristic of gastric carcinoma.
Thus, the use of scout and contrast radiography, ultrasound, possibly endoscopy (not done in the present study) along with appropriate histochemical examination are essential tools in diagnosing gastric carcinoma in dogs.

REFERENCES


