Case Report

METASTASIS OF MAMMARY CARCINOMA TO MYOCARDIUM IN A DOG: CLINICAL AND MORPHOLOGICAL CORRELATION

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Abstract

A case of a widespread neoplastic process, originating from the mammary gland in mongrel bitch, weighing 27 kg and aging 7 years, was described. In the patient, blood morphology, blood biochemical parameters, gasometry of arterial blood, chest X-ray, and heart ECG and USG were determined. ECG record demonstrated elevation of ST-T segment by 0.2-0.3 mV in I, aVL leads and a downwarsloping depression in III and aVR leads. The alterations pointed with high probability to infarction in the lateral wall of the left ventricle. Following demonstration by imaging tests of numerous tumours in the chest, the dog was subjected to euthanasia. Upon autopsy, apart from the primary tumour in the mammary gland, numerous tumours were demonstrated in inner organs, including myocardium. Histopathology confirmed neoplastic growth of adenocarcinoma type. In the vicinity of the tumour localised in the left cardiac ventricle, microscopic examination disclosed regions of cardiomyocyte necrosis, which corroborated the preliminary diagnosis of infarction.

Key words: dog, mammary adenocarcinoma, myocardial infarction, myocardial metastasis.

Neoplasms of the mammary gland in bitches, as well as skin tumours, belong to the most frequent hyperplastic lesions in this animal species (4, 5, 7, 10), and the number of diagnosed cases, particularly of their malignant forms, continuously increases (1). In principle, the site of origin within the mammary gland may involve any cells, including cells of vesicular epithelium, ducts, connective tissue, and myoepithelial cells. This leads to extensive histological variability of neoplastic lesions within the organ and, in many occasions, to diagnostic difficulties. In most cases, the lesions are localised in the posterior pair of the mammary glands with a decreasing tendency in the cephalic direction (15, 17, 20). In the first pair of the mammary glands, neoplastic lesions were detected in only around 33% cases (17). It should be noted that localisation of a malignant tumour in the last pair of the mammary gland represents a very unfavourable prognostic factor. According to the studies of Szczubiał et al. (17) over 63% bitches with so localised tumour died or were subjected to euthanasia due to metastases and/or local relapse within 24 months after excision of the tumour. Most frequently, the disease appears in older animals (as a rule in over 5 year-old ones) and peak incidence is noted in the 9th-11th year of dog’s life (2-4, 6, 12, 17, 18, 20).

In the course of its development, mammary carcinoma, similarly to other malignant tumours, may infiltrate the neighbouring tissues and form metastases to regional lymph nodes and to distant organs. Mammary carcinoma represents a tumour of a high propensity for haematogenic dissemination. Probability for such a dissemination increases if earlier metastases to lymph nodes have been detected. It should be added that in some cases, distant metastases develop, which have not been preceded by metastases to locoregional lymph nodes (9). In women, metastatic foci of breast cancer can develop in any organ, although they are most frequent in bones, lungs, and liver (8, 9). In view of the localisation, breast cancer metastases can be divided into those I - in the osseous system, II –in soft tissues (skin, subcutaneous tissue, lymph nodes), and III - in visceral...
organs (mainly lungs, liver, pleura, adrenal glands, ovary, and brain) (9).

Both in women and in bitches, excision of the original mammary tumour leads to a cure, even in cases of its histologically confirmed malignancy, providing that no metastases have developed and appropriate therapeutic procedure has been implemented. The problem appears when before surgery, the tumour cells have already disseminated in the body and the cells have formed metastatic foci or regional relapse of the tumour has developed in the postoperative scar. In contrast to women, the metastases of mammary cancer in dogs do not develop so frequently. If they appear, they develop in the lungs, regional lymph nodes, including subinguinal, sternal, and prescapular lymph nodes, less frequently in the liver, uterus, urinary bladder, or bones (14, 16). According to Yamagami et al. (19), only 36% of bitches with metastases to locoregional lymph nodes and almost 14% with metastases to internal organs survive two-year post-operative period, while absence of the metastases increases the proportion of animals surviving the period up to over 90%.

Myocardial ischaemia represents frequent pathology in humans. Most frequently, it results from the common, in particular in elderly individuals, arteriosclerosis of coronary vessels. In dogs, emboli in coronary vessels are very infrequent, and result most frequently from endocarditis, less frequently from sepsis or pulmonary tumours (13). In dogs, microscopic intramural myocardial infarctions have been described (MIMI). They may affect as many as 50% dogs above 16 years of life (11). The lesions are localised in the region of the left ventricle papillary muscles, and are probably linked to myxomatotic degeneration of mitral valve (endocardiosis). However, MIMI do not manifest themselves in ECG records in the form of elevated ST-T segment, as it has been in the case of presently described one, and their clinical significance has not been recognised till now (11).

### Description of the case and discussion

A mongrel dog, a 7-year-old bitch, weighing 27 kg was admitted for stationary treatment in the Chair of Internal and Parasitic Diseases with Clinic of Diseases of Horses, Dogs, and Cats, Faculty of Veterinary Medicine. In the mammary gland, a large tumour was detected between the two posterior pairs of the mammary glands. Clinical examination documented cyanosis of mucous membranes, capillary filling time <3 s, weak vesicular murmur over lungs, soft heart sounds, and poorly detectable rhythmic pulse (140/min). The planned surgical removal of the tumour was preceded by blood morphological and biochemical tests (Table 1), gasometry of arterial blood (Table 2), chest X-ray, and ECG and USG examination of the heart.

#### Table 1
Blood morphological and biochemical tests

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measured value</th>
<th>Reference value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytes (G/L)</td>
<td>24.9&lt;sup&gt;*&lt;/sup&gt;</td>
<td>6.0-15.0</td>
</tr>
<tr>
<td>Erythrocytes (T/L)</td>
<td>4.69&lt;sup&gt;*&lt;/sup&gt;</td>
<td>5.5-8.9</td>
</tr>
<tr>
<td>Haemoglobin [mmol/L]</td>
<td>7.0&lt;sup&gt;*&lt;/sup&gt;</td>
<td>7.4-11.8</td>
</tr>
<tr>
<td>Haematocrit (l/L)</td>
<td>0.37</td>
<td>0.37-0.55</td>
</tr>
<tr>
<td>Blood platelets (G/L)</td>
<td>441</td>
<td>150-500</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>37</td>
<td>1-37</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>49</td>
<td>3-50</td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>9.1&lt;sup&gt;*&lt;/sup&gt;</td>
<td>3.32-7.47</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>169&lt;sup&gt;*&lt;/sup&gt;</td>
<td>88.4-150.3</td>
</tr>
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<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measured value</th>
<th>Reference value</th>
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<tbody>
<tr>
<td>pH</td>
<td>7.34</td>
<td>7.35-7.46</td>
</tr>
<tr>
<td>pCO₂ (mmHg)</td>
<td>37</td>
<td>30.8-42.8</td>
</tr>
<tr>
<td>pO₂ (mmHg)</td>
<td>35</td>
<td>80.9-103.3</td>
</tr>
<tr>
<td>HCO₃&lt;sup&gt;-&lt;/sup&gt; (mmol/L)</td>
<td>22</td>
<td>18.8-25.6</td>
</tr>
<tr>
<td>BE (mmol/L)</td>
<td>-2.5</td>
<td>±2.0</td>
</tr>
</tbody>
</table>

Gasometric examination was conducted on the blood, taken from the femoral artery. In the sample of the blood, parameters of acid/alkaline balance were tested, including pH, partial blood pressures of CO₂ and O₂, concentration of HCO₃⁻ as well as excess or deficiency of plasma buffering alkali (BE). The observed decrease in pH of arterial blood and deficiency of plasma buffering alkali (BE) unequivocally pointed to the development of acidosis. Since both the respiratory component, pCO₂, and the metabolic component, HCO₃⁻, of acid/alkaline equilibrium fitted the normal ranges, the acidosis could not be diagnosed as a metabolic or a respiratory one. However, it could be assumed with high probability that due to the very low partial pressure of O₂, probably resulting from impoverished gas exchange in the lungs that the condition would develop into acidosis of the respiratory type. Chest X-ray demonstrated in lungs numerous of apneumatic tumours (Fig. 1).

ECG documented rhythmic sinusoidal contractions 140/min, P wave = 0.04 s/+0.2mV; PQ distance = 0.1 s; QRS ventricular complex = 0.06 s; R wave amplitude = 17 mV, QT distance = 0.18 s, T wave = 0.04 s, two-humped of a positive and negative amplitude (-) 0.1 mV; (+) 0.1 mV. Moreover, ST-T segment was elevated by 0.2-0.3 mV in I aVL lead, while a downward-sloping depression was noted in III and aVR leads (Fig. 2). The alterations pointed with high probability to myocardial infarct in lateral wall of the left ventricle. The average electric vector of the heart was −270. Intraventricular conduction was also non-specifically disturbed.

Echography (Fig. 3) demonstrated normal structure and contractility of the left ventricle within a normal range (shortening fraction (SF)=12.2%, ejection fraction of the left ventricle (EF)=27%). Moreover, enlargement of the right ventricle and slight enlargement of the left atrium was detected. It should be added that the examination disclosed also a hyperchogenic element in the region of papillary muscle in the left ventricle.

Due to numerous tumours in the chest, the dog owner decided that the dog should be subjected to euthanasia and autopsy. The autopsy disclosed a tumour of the left posterior mammary gland (Fig. 4). Lungs contained disseminated tumours of various sizes, up to 3 cm diameter (Fig. 5).

In apical portions of the lungs, large tumours prevailed. In some places, parietal pleura formed adhesions with the neoplastically infiltrated pulmonary lobes. Bronchial and mediastinal lymph nodes were clearly enlarged and hyperaemic. Pericardial sac contained small amount of bloodstained fluid. At the surface of the pericardial sac, a tumour was disclosed of 3 cm in diameter. The left cardiac ventricle contained tumour of 1.5 cm in diameter, protruding to ventricular lumen and, at the base, infiltrating the myocardium (Fig. 6). On the left-hand side, parietal peritoneum contained a tumour of 5 cm in diameter. The liver was markedly enlarged, with blood congestion and brittle parenchyma. The right kidney contained disseminated small tumours of a variable diameter, which infiltrated cortex and medulla and occasionally protruded over the capsule surface (Fig. 7).

The left kidney contained a tumour of around 4 cm in diameter, filled with urine and several small nodules. The spleen was enlarged, swollen, with individual hypertrophic nodules. Inguinal and axillary lymph nodes were swollen and hyperaemic.

In macroscopic examination of the neoplastic growth of the mammary gland, a tumour of 6x10 cm in size was disclosed, with an evidently ulcerated surface of 1.5 cm in diameter. At its base, the tumour deeply infiltrated the surrounding tissues, which significantly restricted its relocability against the sublayer. It manifested a rather solid consistency while its cross-section surface manifested lobular structure and a whitish-creamy colour. In some places, haemorrhagic foci and grey foci of necrosis were noted.

Samples of the tumour were fixed for 24 h in buffered 7% formalin, processed routinely to paraffin blocks, and cut to 4 µm thick sections. In histopathological evaluation of haematoxylin and eosin stained preparations, classification of mammary gland tumours and dysplasia according to WHO was used.

Microscopic examination of the mammary gland tumour permitted to classify it as the adenocarcinoma. Its numerous ducts and follicles were mostly tightly filled with proliferating cells of the neoplastic epithelium (Fig. 8).

Occasionally, the cells formed layers, and characteristic papillae but regions of a solid structure and marked cellular chaos were also present. In several places, basement membrane of vesicles and ducts was interrupted, and the tumour cells infiltrated the mesenchymal stroma of lobules. The cells manifested an extensive atypia and augmented mitotic activity, expressed by numerous cell divisions, including abnormal mitoses. Frequently, extensive regions of necrosis were encountered (Fig. 9) with deposition of calcium salts (Fig. 10), haemorrhagic foci (Fig. 11), and inflammatory infiltrates with prevailing acidophilic granulocytes and, occasionally, mast cells (Fig. 12).

In addition, the structure of the mammary gland tumour contained individual colonies of actinomyces (Fig. 13) surrounded by an inflammatory infiltrate consisting mainly of acidophilic granulocytes. This Gram-positive rod probably penetrated the tumour through the damaged tumour-overlaying skin.

Cells of the same type as those in the mammary tumour were detected also in the inguinal lymph nodes (Fig. 14), lungs (Fig. 15), kidneys (Fig. 16), and in the myocardium of the left ventricle (Fig. 17).

Microscopic pattern of the metastases presented a solid structure of neoplastic cells with evident atypia, numerous mitoses, and a variable intensity of inflammatory infiltration. Moreover, the myocardium of the left ventricle demonstrated focus of coagulative necrosis of cardiomyocytes close to the tumour (Fig. 18).
Fig. 1. Chest radiogram in lateral projection demonstrating numerous atelectatic tumour lesions.

Fig. 2. ECG record with elevation of ST-T segment by 0.2-0.3 mV in I, aVL leads.

Fig. 3. Echography of the heart. Projection in the short birefringent axis. Hyperechogenic element is noted in the vicinity of the papillary muscle of the left ventricle.

Fig. 4. Tumour of the posterior mammary gland.

Fig. 5. Numerous metastatic tumours in lungs.

Fig. 6. Tumour in left cardiac ventricle.

Fig. 7. Metastatic tumours in right kidney.
Fig. 8. Mammary adenocarcinoma. 400x

Fig. 9. Region of necrosis in the mammary tumour. 400x

Fig. 10. Deposition of calcium salts in necrotic parts of the tumour. 200x

Fig. 11. Massive haemorrhagic foci in the tumour. Inflammatory infiltrates in the tumour. 400x

Fig. 12. Necrotic region consisting of granulocytes and mast cells. 400x

Fig. 13. Colonies of actinomyces surrounded by inflammatory infiltrate. 400x

Fig. 14. Metastasis of mammary adenocarcinoma to the lymph node. 400x

Fig. 15. Metastasis of mammary adenocarcinoma to the lungs. 200x
The detection, following thoracotomy, of numerous metastases in the lungs, resulted in atelectasis and relative insufficiency of the lungs, as manifested by acidosis and enlargement of the left ventricle. Anaemia diagnosed by blood tests, probably reflected bleeding from the tumours, while leukocytosis resulted from inflammatory reactions, which accompanied metastases in the kidneys, lungs, and lymph nodes. The metastatic tumour located in lateral wall of the left cardiac ventricle was of a high clinical significance. In the vicinity of the tumour regions, cardiomyocyte necrosis was observed. The myocardial necrosis in the lateral wall manifested itself in ECG record by lowered ST-T segment in I and aVL leads. The necrosis might have resulted from loss of vascular patency due to emboli of neoplastic cells. Changes in ST-T segment have seldom been described in dogs. If they appear, they are related to ischaemia of entire myocardium and they appear during tachycardia. Foci of ischaemia or necrosis manifested by changes in the level of ST-T segment corresponding to a given cardiac wall are practically not encountered in this species. This is explained by the fact that arteriosclerotic lesions, the principal cause of myocardial infarcts in humans, are practically not seen in dogs. It is highly probable that the described myocardial necrosis was strictly linked to neoplastic process developing in the dog and its locations has reflected the site of metastatic focus in the left ventricle. In addition, inflammatory infiltrates in myocardium in vicinity of the tumour, might have induced non-specific disturbances in intraventricular conductance.

References