INFLTRATIVE FORM OF A TUMOUR IN CARDIAC BASE IN A DOG WITH DILATED CARDIOMYOPATHY: CLINICAL AND MORPHOLOGICAL CORRELATIONS. A CASE REPORT

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Abstract

The case of a 12-year-old boxer dog, with an infiltrating tumour in cardiac base and dilated cardiomyopathy was described. Morphological and biochemical examinations of the blood, ECG, and USG of the heart were performed. In the resting ECG record, atrial fibrillation was detected with rapid action of ventricles. Echocardiography demonstrated distension of all cardiac cavities and a decreased contractility of the left ventricular myocardium. Despite intense treatment, the condition of the dog deteriorated: anaemia and renal insufficiency appeared and asphyxia intensified. At the owners' request, the dog was subjected to euthanasia. On autopsy, a tumour in the cardiac base was detected, which infiltrated the left atrial wall. Histopathology and immunohistochemistry permitted to diagnose neoplastic hypertrophy of chemodectoma type.

Key words: dog, cardiac base, chemodectoma, dilated cardiomyopathy.

Both in humans and in animals primary tumours of the heart are occasionally observed (1, 3, 11, 14, 22, 28). Much more frequently, the myocardium provides a site for the localisation of neoplastic metastases. In humans with a widespread neoplastic process, metastatic foci in the heart are noted in approximately 10% of cases (22). The tumours, which most frequently yield metastases to the myocardium, include lung and mammary cancers, melanomas, lymphomas, and leukemic growth (17, 22). Primary cardiac tumours are estimated to affect around 0.2% of dogs and in most cases, they are of malignant forms (2, 27). The most frequently diagnosed malignant tumours of the organ are angiosarcoma, rhabdomyosarcoma, and chondrosarcoma, while benign cardiac tumours include myxoma, lipoma, and fibroma (14, 22, 27). Similarly to most other tumours, cardiac neoplasms develop more frequently in old individuals. In studies conducted by Ware et al., (27) on 1 383 cardiac tumours, it was demonstrated that the tumours developed most frequently in dogs aged 7 to 15 years. The authors also showed that cardiac tumours appeared with equal frequency in both sexes, but they were slightly more frequent in animals subjected to sterilisation procedures. The predisposition of breeds to cardiac tumours was also demonstrated in German shepherds, golden retrievers, French bulldogs, and boxers. On the other hand, the lesions were only sporadically noted in dachshund, beagle, rottweiler, and Pekingese (27).

Heart base tumours form one of subgroups among cardiac tumours. The group includes both neoplastic tumours within ectopic glandular tissue of the thyroid or parathyroid and tumours of aortic body, the so-called chemodectomas.

Description of the case and Discussion

A 12-year-old boxer was referred to the Clinic due to frequently appearing disturbances in balance, loss of consciousness, and rapidly reduced exertional capacity. Clinical examination documented cyanosis of mucosal membranes, capillary filling time of 4 s, and
dull, accelerated, and irregular cardiac sounds. Blood morphological and biochemical studies demonstrated
12.0 G/L leucocytes; 7.9 T/L erythrocytes; 9.1 mmol/L haemoglobin; haematocrit of 0.44 l/L; activity of alanine
aminotransferase 39 U/L, activity of aspartate aminotransferase 36 U/L, creatinine concentration of 151 µmol/L, and urea concentration of 4.3 mmol/L.
Resting ECG demonstrated atrial fibrillation with rapid action of ventricles, reaching 240-260 contractions/min (Fig. 1).

In the echocardiographic examination, all cardiac cavities were found dilated and the myocardium of the left ventricle showed a decreased contractility. In vascular projection, diameter of the aorta (Ao) amounted to 2.1 cm, and diameter of the left atrium (LAA) was 5.1 cm. In the four-cavities projection, in the long axis diastolic dimension of the left ventricle (LVd) amounted to 4.8 cm, and its systolic dimension (LVs) was 3.8 cm. In diastole, interventricular septum was 1.0 cm thick (IVSd), and the same thickness was manifested by the septum in systole (IVSs). In diastole, free wall of the LVd was 1.0 cm thick and in systole, it was 1.5 cm thick. The echocardiographic parameters allowed calculating the shortening fraction (SF) of 18.5% and the ejection fraction (EF) of 38%. Echocardiographic examination demonstrated no tumour lesions. In the treatment of the dog, 0.25 mg of Digoxin and 0.5 mg/kg b.w of Metoprolol prolongatum were applied once daily. Control ECG examination showed a slowing down of the ventricular rhythm to 160/min, and the echocardiographic examination demonstrated improved contractility (SF=28%, EF=54.2%). After three months of the treatment, the condition of the dog suddenly deteriorated, the dog thrice lost consciousness. A 24 h-ECG examination according to Holter demonstrated attacks of non-stable ventricular tachycardia (nsVT). Digoxin administration was discontinued, and Pimobendane in a 10 mg dose twice daily was introduced while the dose of Metoprolol was increased to 1 mg/kg b.w. Despite the intense treatment, ascites and hydropericardium developed in subsequent weeks. The ascites fluid was drained, and loop diuretic drugs (Furosemide), thiazide diuretic drugs (hydrochlorothiazide), and potassium-saving diuretics (Furosemide), thiazide diuretic drugs (hydrochlorothiazide), and potassium-saving diuretics were introduced. Unfortunately, anaemia soon appeared (Hb=6.3 mmol/L, haematocrit=0.34 l/L, erythrocytes 4.9 T/L), renal failure developed (serum creatinine 276 µmol/L urea 19.3 mmol/L), and dyspnoea was increasing severely. On the owners’ request, the dog was subjected to euthanasia. Autopsy demonstrated the continuity with adventitia of the aorta, and in parallel infiltrating the wall of the left atrium (Fig. 2).

The tumour was covered by a connective tissue capsule with evident rich network of blood vessels. The tumour’s surface was uneven, with multiple invaginations. On the cross-section, individual haemorrhagic foci and large central necrotic area were noted. Sections were taken for histopathological examination. They were fixed in buffered 7% formalin. A routine staining with haematoxylin and eosin was performed. Histopathological examination showed neoplastic hypertrophy of chemodectoma type, qualified as malignancy of 3rd degree according to Brown et al. (3). The neoplastic cells formed numerous foci of a variable size, separated by strongly branched and supplied with rich blood vessels, with bands of connective tissue (Fig. 3).

Most of the cells demonstrated a polygonal outline, with round or oval cell nucleus, and individual nucleoli. Mitotic figures were not very frequent. Finely granular cytoplasm contained vacuoles of variable size and shape. The typical trait of the tumour involved extensive polymorphism of cell nuclei and their hyperchromasia (Fig. 4).

Moreover, a rich blood supply was evident, with numerous muscular arterioles, thin-walled veins and a network of fine capillaries within connective tissue septa. In some regions of the tumour, the cells arranged themselves in a radial manner around blood vessels (Fig. 5).

Microscope examination demonstrated also diffuse areas of haemorrhages and an extensive region of necrosis in the tumour centre (Fig. 6). In the peripheral parts of the tumour fine inflammatory infiltrates were noted, consisting mainly of lymphocytes and histiocytes.

In order to verify results of the standard histopathological examination, immunohistochemistry was used applying a panel of antibodies capable of identifying neoplastic cells of neural and neuroendocrine origin (6, 13, 20). The panel consisted of three monoclonal antibodies, against chromogranin A (clone DAK-A3, product diluted 1:100, DakoCytomation), synaptophysin (clone SY38, product diluted 1:20, DakoCytomation), and neuron-specific enolase (NSE) (clone BBS/NC/V1-H14, product diluted 1:150, DakoCytomation). All the reactions yielded positive result in the form of a fine-granular brown product, localised mainly in the cytoplasm of tumour cells (Figs 7-9), which corroborated the preliminary diagnosis.

Apart from the tumour samples, histopathological examination included also samples of parenchymatic organs. In the liver evident reconstruction of parenchyma was detected, with obliteration of lobular architecture of the organ. Moreover, a large haemorrhagic focus was detected, with the destruction of hepatocytes and accumulation of haemosiderin and bile pigments in its peripheral parts (Fig. 10).
Fig. 1. Electrocardiographic record demonstrating atrial fibrillation with rapid action of ventricles. Tape feed: 50mm/s, 1mV=10mm.

Fig. 2. Chemodectoma cells infiltrating the myocardium. HE, 400x

Fig. 3. Foci of neoplastic cells separated by bands of connective tissue well supplied with blood. HE, 400x

Fig. 4. Polymorphism and hyperchromasia of cell nuclei in chemodectoma. HE, 400x

Fig. 5. Chemodectoma cells radially arranged around blood vessels. HE, 400x
Fig. 6. Regions of haemorrhage and necrosis in the tumour centre. HE, 200x

Fig. 7. Expression of chromogranin A in cytoplasm of chemodectoma cells. 400x

Fig. 8. Expression of synaptophysin in cytoplasm of chemodectoma cells. 400x

Fig. 9. Expression of neuron-specific enolase (NSE) in cytoplasm of chemodectoma cells. 400x

Fig. 10. Haemorrhagic focus in the liver. HE, 200x

Fig. 11. Interstitial inflammatory infiltrates in the kidney. HE. 200x
In the kidneys, non-purulent interstitial inflammation was detected with numerous foci of mononuclear cell infiltrate, with lesions of parenchymatous and fatty degeneration type in epithelium of renal tubules (Fig. 11). In addition, renal cortex contained fine foci of fibrosis.

In the lungs, regions with pronounced alveolar emphysema (Fig. 12) and non-suppurative inflammatory infiltrates located in the wall of bronchioles and around them (Fig. 13) were detected. Oedema and congestion of pulmonary tissue were also evident, with the presence of erythrocytes in the lumen of alveoli (Fig. 14).

Tumour of aortic body and carotid body, termed paraganglioma or chemodectoma or glomus tumor, develops at the site of anatomic manifestation of aortic/carotid bodies. The tumours originate from neurogenic cells of the chemoreceptor type. Under physiological conditions, the cells are sensitive to alterations in CO₂ and pH levels in blood, as well as to partial pressures of oxygen and in this way they participate in the mechanisms controlling circulation and respiration processes (24). The most frequent localisation of such tumours in humans, involves the bifurcation of internal carotid artery, superior bulb of the jugular vein, less frequently tympanic cavity, and inferior vagal ganglion (19). In animals, the tumours develop most frequently in the form of a single neoplasm, less frequently in the form of numerous fine nodules, located by the base of the heart, within the pericardial sac (9). In the majority of the cases, the tumours manifest continuity with adventitia of the pulmonary artery or ascending aorta (14). Considering all animal species, tumours of chemodectoma type are encountered most frequently in dogs and small bulldogs are thought to be particularly predisposed to develop the tumour (7, 21). Pathogenesis of the tumour development is thought to involve chronic hypoxia, reflecting architecture of upper respiratory pathways in brachycephalic dogs, which leads to hypertrophy and finally neoplastic transformation of the chemoreceptor cells (1, 28). Similarly, enhanced predisposition to development of such tumours of chemoreceptor tissue was detected in humans and animals inhabiting high mountains where the partial pressure of oxygen is lowered (14). Chemodectoma usually occurs as a non-malignant tumour, growing by expansion and in rare occasions only infiltrating the surrounding tissue and yielding metastases mainly to the lungs, liver, myocardium, brain, and bones (1, 4, 5, 10, 15, 21, 23).

In the discussed case, despite the histologically malignant character of the tumour, no metastases were detected but renal insufficiency and anaemia provided a significant problem. They developed in the course of cardiac insufficiency due to dilated cardiomyopathy, resulting in the pattern of cardio-renal anaemia syndrome (CRA). Anaemias developing in the course of chronic diseases comprise in dogs a significant group among anaemias. Anaemias accompanying chronic renal insufficiency and anaemias associated with neoplastic processes dominate in the group. The most frequent cause involves disturbed haematopoesis linked to a disturbed synthesis of erythropoietin (Epo). The most frequent signs of anaemia include weakening, pale mucous membranes, tachycardia, and dyspnoea, which were intensified in the discussed dog with the development of anaemia. Disturbances in erythropoietin production and its considerably insufficient secretion are responsible for the development of anaemia in the course of chronic renal insufficiency. Haemolysis also plays a significant role, which frequently accompanies
chronic renal failure and results from destructive effects of uraemic toxins on erythrocytes. The toxins shorten the survival of erythrocytes and intensify their destruction both in the blood vessels and in the spleen. In some cases, the anaemia seems to be aggravated also by an impoverished response of bone marrow to Epo, by a deficiency in iron, folic acid, or vitamin B₁₂, and by occult bleeding to the alimentary tract, which may accompany chronic renal failure. Due to the progressive haemodynamic alterations in the circulation, which result from anaemia, the latter has been accepted to represent an independent factor, which modulates mortality of patients with congestive circulatory insufficiency (8). A decrease in the Hb concentration by 1 g% is known to augment the risk of hypertrophy in the left ventricular myocardium by 6% (12). A decreased blood viscosity and a decreased resistance to circulation in anaemia, which accompanies congestive heart failure reflecting chronic anoxia, result in a development of hyperkinetic circulation, in which the cardiac output is high, despite the low arterial blood pressure (16). Interaction between anaemia, congestive cardiac insufficiency, and chronic renal failure create the so-called vicious circle, as they deteriorate cardiac work and renal function and intensify the degree of anaemia. Chronic renal failure, congestive cardiac insufficiency, and anaemia are strictly inter-related to each other and they are termed the syndrome of cardiac-renal anaemia (8, 18, 25, 26).

In summing up the data on the discussed case, it may be assumed that the congestive heart insufficiency due to dilated cardiomyopathy was additionally complicated by the neoplastic process in the wall of the left atrium, resulting in renal insufficiency and anaemia.

References