LIVER METASTASES IN MAMMARY CARCINOMA IN FEMALE DOGS: CASE STUDY

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ABSTRACT

At female dogs, the malign tumors have metastases potential, both on lymphatic way at the regional lymphatic nodules, as well as on sanguine way, on the lungs or in distant places of the body, including liver, spleen, heart and boned system.
This case study presents a half-blood female dog, 11 years old, with mammary tumors at the level of the right mammary chain (M_5) and partial mastectomy (M_3, M_4, M_5), on the left mammary chain. The clinical examination also underlined ascites, anorexia, diarrhea and severe dyspnoea. The female was undertaking several complementary examinations: ultrasound, radiology, necropsy and histopathology.
The ultrasound examination revealed the presence of liver hypo- and hyperechogenicity. The radiological examination revealed the presence of a large sized radio-opaque area (1.5-2 cm) on the right pulmonary diaphragmatic lobe and on the left cardiac lobe an area of smaller sizes (0.5 cm).
From the necropsy perspective, besides the pulmonary and hepatic lesions revealed following the complementary imagistic examinations, it was revealed the presence of both pancreatic and renal metastases.
The histopathological examination from the mammary lesion revealed the presence of a malignant epithelial tumor, the diagnosis being of complex type mammary carcinoma. The histopathological examination of the liver confirms the fact that the liver metastases have the same origin as the one in the mammary chain.

Key words: *female dogs, liver metastasis, mammary tumors*.

INTRODUCTION

Nowadays, mammary tumours account for 50% of the total neoplasms affecting lady dogs (Daleck et al., 1998, Oliveira et al., 2003). Between 40% and 50% of the mammary gland tunours are malign, and 50% of these may disseminate, following the tract of the lymphatic vessels adjacent to regional lymph nodes and blood vessels (Harvey, 1998; Robbins, 2003; Hedlund, 2007).
Mammary tumoral lesions are easy to identify, and matastases generally occur from a few months to a few years after the discovery of the primary

tumour. The average age for the detection of mammary tumoral lesions is 10 – 11 years old. (Ginn et al., 2007).
The literature in the filed indicates the fact that the lung is the main metastasation spot of mammary tumours (for 60-80% of the cases), but they may disseminate into other organs, as well: lymph nodes, suprarenal glands, kidneys, heart, bones, liver, brain, eyes, nose, spleen, uterus, serous parts (Lagadic and Cohn-Bendit, 1995; Sorenmo, 2003; Muller and Guaguère, 2006; Fontbonne et al., 2007). Occasionally, the skin may also be a metastasation spot of canine mammary tumours, determining cutaneous carcinomatosis (Muller and Guaguère, 2006).
The mammary carcinoma represents a tumour with a high tendency of haematogenous and/or lymphatic dissemination. The probability for such dissemination increases if there have been previously detected metastases at the level of the lymph nodes. Some cases recorded the occurrence of remote metastases, without being preceded by metastases at the level of the lymph nodes (Jassema, 1998).

MATERIALS AND METHODS

The present study is focused on an 11-year old, mixed-breed, lady dog, weighing 27 kg, with mammary tumoral lesions.
The investigations were performed at the Faculty of Veterinary Medicine in Bucharest, the female being subjected to the following protocol:

- The collection of anamnestic data
- Clinical examination: the morphoclinical examination of the primary tumour (identification of the number of affected mammae, the mortification/ulceration degree, the detection of affected lymph nodes).
- Complementary exams:
  - Abdominal ultrasound scan.
  - Lateral and ventro-dorsal pulmonary radiography, using the digitalised radiological technique.
  - During necropsy there have been biological samples collected in view of determining a definitive diagnostic.
  - Anatomopathological examination: macroscopic and histologic tests performed on the samples collected after the necropsy. The tumoral tissue fragments collected in view of performing the histological exam were placed in formaldehyde 10% solution, processed by means of the

classic histopathological method, with an inclusion in paraffin and cutting by section cutter, whereas the colouring methods were the bichromic hematoxilin-eosine (HE) method and the Masson trichromic method.

RESULTS AND DISCUSSIONS

Following the clinical examination, it was ascertained that the female displayed a mammary tumoral lesion located on the right mammary chain (M_5 – inguinal mamma), plus a partial ablation of the left mammary chain (M_3, M_4 si M_5), batrachian abdomen (ascites) and a state of inappetence. In the meantime, the female was subjected to the radiological exam in view of detecting any possible pulmonary metastases.

The *anamnesis* revealed that the primary tumoral lesion had been detected on the left mammary chain – M_5, three years before (2009), measuring approximately one cm. In November 2011, the female underwent a surgical procedure which comprised: sterilisation (OHT - ovariohysterectomy) and partial mammectomy with a tumoral lesion on M_5 (6 cm, hard, immobile).

In January 2012, it also developed on the right mammary chain - M_5 (2 cm, hard and adherent to the neighbouring tissue). At the time of the clinical examination, it measured 5 cm and was hard, adherent and with a bosselated surface (Figure 1).

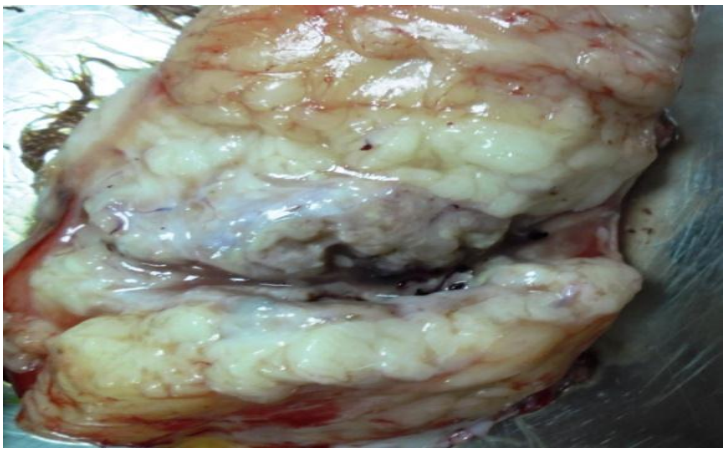

Figure 1. Mammary tumoral lesion M_5, right mammary chain (appearance in section).

Starting from March (2012), the lady dog began breathing heavily (dyspnea), and in April it was subjected to an ultrasound scan, due to the clinical, ascites-like aspect. Following the ultrasound procedure, the following were ascertained: hepatic modifications in the vicinity of the hydroperitoneum (irregular surface, with an alternation of hypoecogenic and hyperecogenic areas, suspicion of hepatic metastases), renal modifications (right kidney – 5,6 cm, left kidney – 5,8 cm, with the corticomedullary limit poorly delimited).

A therapy followed, consisting in the administration of diuretics (furosemide, manitol), hepatic protectors (aspatofort), antibiotherapy (amoxicilin), anti-haemorrhagic medication (etamsilat, fitomenadion, vitamine C), analgesic medication (algocalmin) and theramnekron (with some antitumoral effects).

During its lifetime the lady dog was not administered hormonal medication, it never gave birth, however, there have been multiple false lactations recorded (the ovariohysterectomy took place at a later date, when it was 10-years old). The literature data confirms that both the false lactations and the lack sterilisation led to the risk mammary tumour occurrence (Donnay et al., 1994; Schneider et al., 1969).

Age is one of the predisposing factors in the occurrence of mammary tumoral lesions, the incidence increasing with aging, as was the case in our study (11-years old). Out of the various studies conducted on this subject, the conclusion states that the maximum frequency applies to the 9 – 11-years old interval (Perez Alenza et al., 2000).

The radiological exam confirms the presence of two radiopaque areas at a pulmonary level (on the left diaphragmatic lobe, ⌀ ≈ 1.5 cm and on the right cardiac lobe, ⌀ ≈ 0,5 cm), which may belong to the category of multiple pulmonary metastases. Other conditions recorded were sternal lymphadenopathy, incipient mediastinal reactivity, hypertrophy of the aortic crutch, secondary to the reactivity of the pericardic madiastinal lymph nodes (Figure 2). Vincent (2010) recommends thoracic radiography in order to assess any possible pulmonary metastases and the sternal lymphadenopathy, including them within: single metastases, multiple metastases and interstitial ± peribronchial infiltrate (Vincent, 2010).

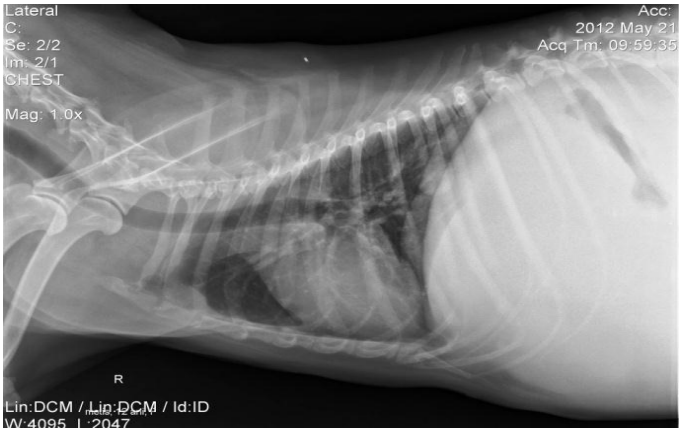

Figure 2. Pulmonary radiography, lateral incidence, confirming the presence of two radiopaque areas (multiple pulmonary metastases), sternal lymphadenopathy, hepatomegaly and hydroperitoneum.

With regard to the T.N.M. (tumour, lymph node, metastasis) classification, the female in the present study falls within the 4^{th} stage (T_4, N_1, M_1), as per the classification of Mangol et al. (1998) (Magnol et al., 1998).

Prior to the euthanasia, the female displayed severe dyspnea, a 4-day old anorexia, increased fever, abdominal colic and diarrhoea. Subsequent to the clinical exam and the additional investigations, a severe prognosis was established and the female was subjected to euthanasia.

After the lady dog's death the *necropsy* was performed, with an emphasis on the presence of pulmonary, hepatic, pancreatic, splenic and renal tumoral formations (macroscopically visible). From a pulmonary point of view, the study identified nodular formations of variable sizes, present both on the right, as well as on the left lung (on the left diaphragmatic lobe, size ≈ 1.5 cm, and on the right cardiac lobe, size ≈ 0.5 cm). These displayed a firm consistency, were compact and with a bacon-like appearance in section, against the lung's greyish-pink background. At the opening of the abdominal cavity a large amount of serosanguinolent liquid was observed (hemoperitoneum) (Figure 3).

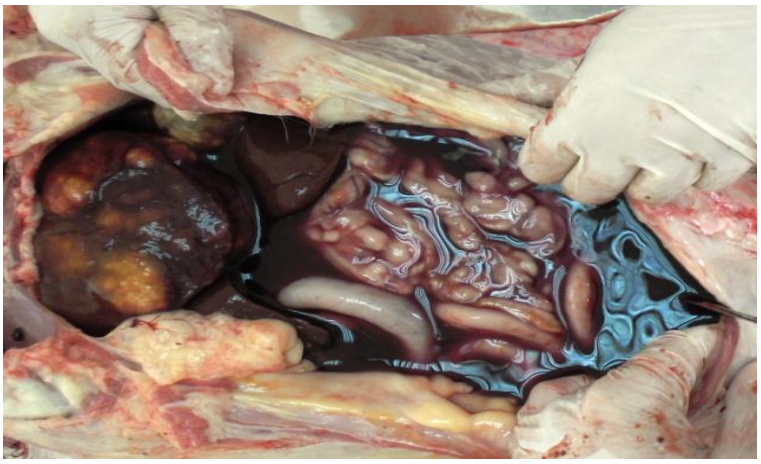

Figure 3. Abdominal laparotomy, emphasizing the hepatic nodular formations and the hemoperitoneum.

The necropsy identified multifocal modular hepatic formations, of variable sizes (ø 2-20 cm), disseminates within the entire liver mass. The right hepatic lobe was the most affected, being the host of a ≈ 20-cm nodule, followed by the right intermediary lobe (ø ≈ 8 cm) and the left lobe, which displayed two nodular formations measuring approximately 6 cm ø, situated at the lobe's poles (Figure 4). These presented a multinodular appearance in section, with a confluation tendency, with greyish-white bacon-like compact areas which alternated with small haemorrhagic areas.

Figure 4. Multifocal nodular hepatic lesions, of variable sizes (hepatic metastases).

The sectioning of the large modules produced a viscous, dirty-greyish liquid. The pancreatic tumoral nodular formations were also disseminated within the entire organ mass. It was noticed, in the lateral-median area of the organ, a pedunculated formation approximately 4 cm in size, firm when palpated. The splenic region revealed a symmetrical splenomegaly with a stasis appearance and multiple greyish-white formations, compact in section, disseminated within the entire parenchyma. The renal region presented bilateral tumoral formations, the renal decapsulation was performed with ease, the left kidney displaying two tumoral formations, one approximately 2 cm in size, located at the cranial pole, with a cystic appearance (which comprises both the cortical area, as well as a part of the medullar area), a smaller one, ≈ 0.5 cm, situated on the dorsal side. A tumoral formation ≈ 1 cm was detected on the right kidney, close to the renal hilum, situated on the dorsal side. The lesional picture led to the suspicion of carcinomatous matastasis, having the mammary gland as a starting point, and was completed by a severe mesenteric lymphadenopathy.
The microscopic (histopathological) *exam* revealed the presence of a malign tumour, the diagnostic being the complex type mammary carcinoma, and confirmed that the remotely detected metastases have the same origin and the same histological pattern as the primary tumour.
The histologic aspects of the primary tumour (M_5 – inguinal mamma) and of the metastases were represented by the characteristic pattern of complex carcinomas, which comprises both epithelial proliferations, as well as proliferations of cells with a fusiform appearance, of mioepithelial origin, which affect both the mammary acini, as well as the ducts. The tumoral proliferation is associated with an inflammatory reaction (neutrophils, macrophages and lymphocytes). Notable aspects were the infiltrative nature of the tumoral cells, numerous clusters of necrosis within the tumoral mass, as well as a relatively high number of mitoses, all these representing high malignity criteria (Figure 5).

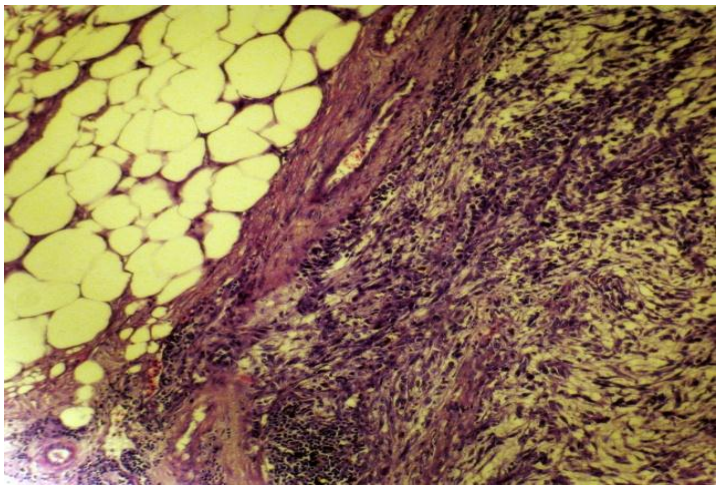

Figure 5. Histopathological exam, complex type mammary carcinoma, 100x.

From a histologic point of view, one can distinguish within the liver mass numerous carcinomatous clusters with a confluation tendency. Even if the tumoral formations seem to be delimited from the conjunctival stroma, it is penetrated by tumoral elements, which endows it with a marked infiltrative nature. The tumoral tissue morphology is heterogeneous, with areas, similar to the primary tumour, where the appearance of complex carcinoma prevails, with randomly positioned epithelial and mioepithelial cells (Figure 6).

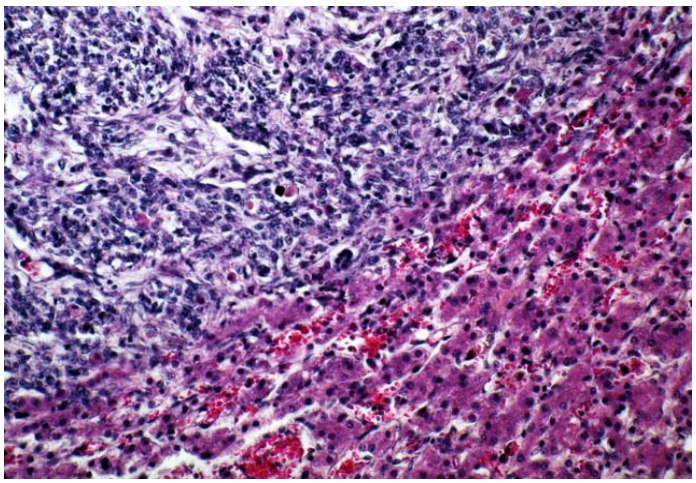

Figure 6. Histopathological exam, hepatic matastasis, 200x.

CONCLUSIONS

The present study was centred around a half-breed female, age 11, with mammary tumours at both chains and an extension of the metastases towards various organs: liver, lung, pancreas and kidney.
The ultrasound examination emphasizes areas with hypo- and hyperecogenity (suspicion of hepatic metastases).
The radiological exam revealed the presence of two radiopaque pulmonary areas of various sizes, included in the type of multiple metastases and, moreover, a sternal and mediastinal lymphadenopathy was identified, whereas the liver presented hepatomegaly and ascites radiological signs.
From a histopathological point of view, it was conformed that the metastases had the mammary gland as a starting point, with an emphasis on the type of complex mammary carcinoma.

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