Signs of metastatic disease on thoracic radiographs of dogs suffering from mammary gland tumours: a retrospective study (1990–1998)

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Summary

A mammary gland tumour (MGT) was clinically diagnosed in 136 dogs. Histologically 71% were malignant and 29% benign. Intrathoracic metastatic disease was noted or suspected radiographically in 13.5% of the dogs with malignant and in 2.5% of the dogs with benign MGT. Six dogs with malignant MGT were necropsied, 5 had pulmonary metastases but only 1 had radiographic signs of intrathoracic metastatic disease. We conclude that radiographs are not very sensitive for detection of early intrathoracic metastatic disease of MGT.

Key words: dog, mammary gland neoplasia, pulmonary metastases, radiology

Zeichen von Metastasen auf dem Röntgenbild von Hunden mit Mammatumoren: Eine retrospektive Studie (1990–1998)

Mammatumoren (MT) bei 136 Hunden waren zu 71% maligne und zu 29% benigne. Radiologisch wurden bei 13.5% der Hunde mit malignen und bei 2.5% der Hunde mit benignen MT intrathorakale Metastasen diagnostiziert oder vermutet. Sechs Hunde mit malignen MT wurden seziert, 5 hatten Lungenmetastasen, aber nur bei 1 fanden sich radiologisch intrathorakale Metastasen. Wir schliessen daraus, dass Röntgenbilder zur Erfassung von intrathorakalen Metastasen bei malignen MT eine geringe Sensitivität aufweisen.

Schlüsselwörter: Hund, Mammatumor, Lungenmetastase, Radiologie

Introduction

Mammary gland tumours (MGT) are the most frequently diagnosed neoplasm in the bitch and account for 13–53% of all the tumours seen (Brodey et al, 1983; Sorenmo, 2003). The median age at the time of diagnosis is 10 to 11 years, however tumours rarely occur before 5 years of age. About 50% of the tumours are considered to be malignant and of these 25–50% have metastases (Cotchin 1958). The most common sites of metastatic malignant MGT are the tributary lymph nodes and the lung (Pereira, 2003). Other sites for metastases are heart, kidney, liver, brain, skeletal muscles, adrenal glands, spleen, pancreas and diaphragm (Brodey et al., 1983). Survival time is mainly dependent on the histological subtype, evidence of metastasis at the time of diagnosis and tumour size (Philibert et al., 2003).

Pulmonary metastases may be detected radiographically. Thoracic radiographs taken in lateral recumbence impair inflation and cause overperfusion of the dependent lung lobes, resulting in an increased radiopacity and a reduced contrast between pulmonary parenchyma and neoplastic nodules located in these lobes. As a result, focal pulmonary consolidations or nodules may not be visible (Forrest, 1992). Therefore, either a two-view protocol (right and left lateral recumbent) with two readers examining the radiographs, or a three-view protocol (with an additional ventrodorsal projection) with only one reader examining the films is recommended (Lang et al., 1986). Alternatively, two orthogonal views are recommended. However, even a single lateral projection of the thorax may be adequate in detecting pulmonary metastases in dogs, if there are metastases in multiple lung lobes or if the metastases are large (Barthez and others, 1994). The purpose of our study was to define the incidence of radiographically visible pulmonary metastases in dogs with MGT at the time of presentation and to correlate the type of tumour and incidence of pulmonary metastases.

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Animals, Material and Methods

Medical records of dogs suffering from MGT seen at the section of Small Animal Reproduction, University of Zurich, from 1990 to 1998 were reviewed. Only dogs with a cytologically or histologically confirmed diagnosis of MGT and isochronal radiographic assessment of the lung were included in this study. Results of histological examination of the excised tumours from 134 dogs and of biopsy samples from tumour tissue from 2 dogs were available. Six of these dogs were dissected. The tumours were classified histologically according to the classification system of Moulton (1990).

Radiographs of the lung taken in right and left lateral recumbence were available from all dogs. Radiographs were taken using a T6 screen and a XLA film combination (Kodak). Film-focus distance was 115 cm and focal spot size was 1.1 mm. Radiographs of patients with a thoracic diameter of up to 15 cm were taken in tabletop technique. For larger patients a moving grid (12:1) was used. The radiographs were interpreted independently by two radiologists.

Results

The dogs were from 43 different breeds and a variety of mixed breeds. The median age at time of diagnosis was 10 years, ranging from 1 to 17 years. 121 bitches were intact, 15 were spayed. No abnormalities were noted on thoracic radiographs of 122 dogs, while intrathoracic pathology was found in 14 dogs (Tab. 1). Nodular radiopacities considered to be pulmonary metastases were seen in 5 dogs (Fig. 1). They all had malignant MGT. Metastatic MGT was suspected in the remaining 9 dogs, 8 of which had malignant MGT. The radiographic findings were increased reticular, peribronchial and miliary opacities, or an ill defined pulmonary mass (Fig. 2). In addition, sternal lymph node enlargement was noted in 3 dogs (Fig. 3). One had pleural effusion (Tab. 2).

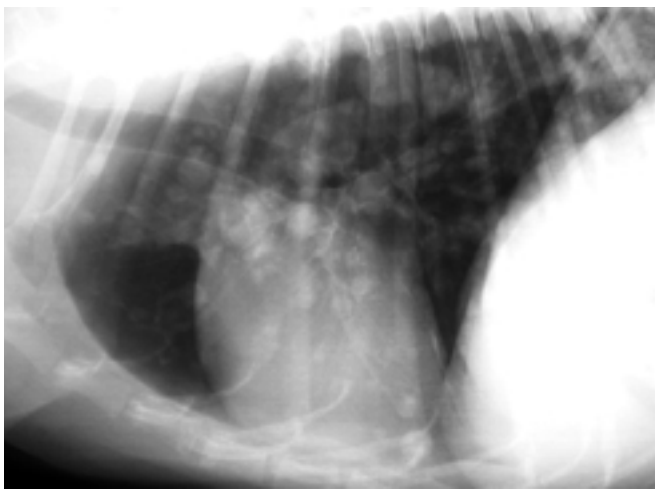

Figure 1: Collie, 13 years old, diagnosed as mammary fibrosarcoma. Multiple well marginated pulmonary opacities are compatible with pulmonary metastases.

Table 1: Relation between histological type of MGT and abnormalities on thoracic radiographs.

Histological type of MGT	Abnormal findings on thoracic radiographs	
	n	%
malignant	13/96	13.5
carcinoma	9/61	14.8
mixed	4/32	12.5
sarcoma	0/3	0
benign	1/40	2.5
mixed	1/38	2.6
adenoma	0/2	0

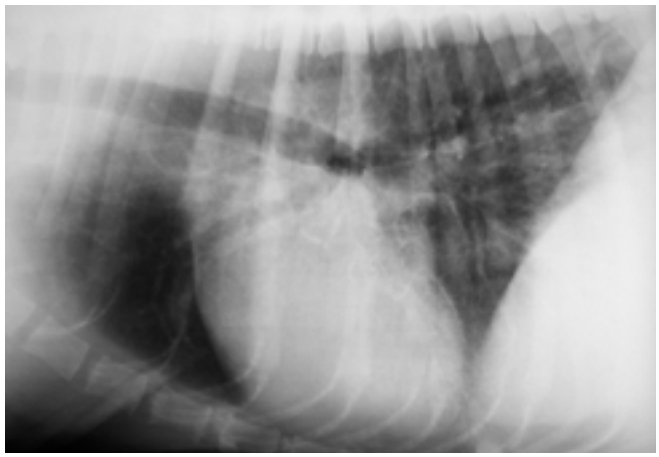

Figure 2: Belgian Shepherd dog, 8 years old, diagnosed as mammary adenocarcinoma. The disseminated increased reticular pulmonary opacitiy is suspicious for widespread pulmonary metastases or severe pulmonary fibrosis. No histological examination of the lungs was performed.

On histological examination 96 dogs had malignant tumours in one or several mammary gland complexes, and 13 (13.5 %) of them showed radiographic evidence or suspicion of intrathoracic metastatic MGT. Histological diagnosis was mammary gland carcinoma in 9 and malignant mixed tumours in 4 dogs. The other 40 dogs had benign MGT. In one of them (2.5 %) an increased interstitial pulmonary pattern was noted on radiographs and categorised as suspected intrathoracic metastases. Histological details of all tumours are listed in table 1.

Necropsies were performed on 6 dogs with malignant MGT. Pulmonary metastases or micrometastases were noted in 5. The thoracic radiographs were interpreted as normal in three of them, classified as slightly increased interstitial pulmonary pattern not diagnostic for pulmonary metastases in one, and sternal lymphadenomegaly compatible with neoplasia in one

Table 2: Abnormal radiographic findings in 14 of 136 dogs with MGT.

Radiographic findings (single or combinations)	Affected dogs	Malignant MGT (n = 13)	Benign MGT (n = 1)
pulmonary nodules	5	5	0
peribronchial opacities	3	2	1
micronodular opacities	2	2	0
reticular opacities	1	1	
single ill defined pulmonary opacity	2	2	0
enlarged sternal lymph node	3	3	0
pleural effusion	1	1	0

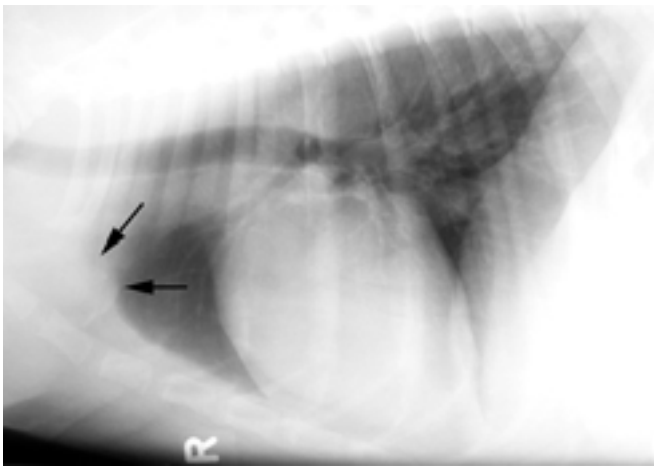

Figure 3: Appenzell Mountain dog, 7 years old, diagnosed as malignant mixed tumor. The enlarged sternal lymph node (arrows) is compatible with metastatic spread of the mammary gland neoplasia. Differential diagnosis is severe mammary gland inflammation/infection.

dog. One dog was free of pulmonary metastases, established radiographically and at necropsy.

Discussion

Canine malignant MGT readily metastasise to distant organs. Fidler and Brodey (1967) reported organ metastases in 93 of 100 dogs with malignant MGT confirmed at necropsy. The most frequently encountered metastatic site was the lung, identified in 83%. As most pulmonary metastases were located in the interstitial tissue rather than in the alveolar or bronchial tissue of the lung, they rarely produced clinical signs. In our study 71% of the reviewed MGT were histologically diagnosed to be malignant, approximately 20% more than that reported in a recent literature review (Sorenmo, 2003). The University of Zurich veterinary clinic is a referral clinic and may therefore receive more patients with aggressive or recurring MGT than private practitioners. The exact percentage of dogs developing tumour recurrence could not be evaluated from the case histories.

Radiographic prevalence of intrathoracic MGT metastases in our study was low. It was noted or suspected in 13.5% of the dogs with malignant MGT and suspected in 2.5% with benign MGT. The precise percentage of false negative radiographic diagnoses could not be derived as only 6 dogs were necropsied. The radiographs of only 1 of these 6 dogs were interpreted to be positive and of another 1 as suspicious for pulmonary metastases. These numbers are small but indicate that the sensitivity of radiographic examination for correctly detecting pulmonary metastases is disappointingly low. The radiological accuracy (probability to recognize a pulmonary nodule on radiographs) for a 3-view radiographic protocol of the thorax is 97 to 100% while for a 2-view protocol with left and right lateral recumbence it is 95 to 100% depending on the number of readers (Lang et al., 1986). This figures merely indicate that radiology is an accurate method for the detection of pulmonary metastases of a minimal size. The true sensitivity of thoracic radiographs for detecting any size of pulmonary metastases may be much lower and has been calculated to be as low as 65% (Suter et al., 1974; Tiemessen, 1989; Djupsjöbacka et al., 2001). A single nodule must have a minimal diameter of 4 mm to be detectable on radiographs. Smaller nodules are referred to as micronodular or miliary nodules. They are usually not perceived as single opacities but rather blend into the diffuse interstitial background (Suter, 1984). They are therefore not interpreted as a sign of neoplastic disease unless present in large numbers.

Nodular opacities noted on radiographs in 5 dogs were considered to be pulmonary metastases. Possible differential diagnoses are primary pulmonary neoplasm, granuloma, cyst, or abscess formation, all of which are rare in Switzerland. Also to be considered are pulmonary vessels seen on end and extrathoracic densities superimposed on the lung parenchyma, such as nipples, pendulous skin tumours and ticks. They are usually easy to detect on palpation. Large numbers of small nodules may reflect a miliary infection, pulmonary infiltrates with eosinophils (PIE), or a hypersensitivity reaction secondary to infection with Dirofilaria immitis (Suter, 1984). The incidence of Dirofilariosis is very low in northern Switzerland (<0.2% of all dogs necropsied). Therefore, in the presence of MGT the probability of an unrelated disease is low.

The enlarged sternal lymph nodes in 3 dogs were interpreted as suspicious for intrathoracic metastatic MGT disease. Enlarged sternal lymph nodes may result from diseases of the peritoneum, the cranial abdominal organs or the abdominal or thoracic wall.

The mammary gland complexes I, II and III usually drain to the axillary lymph nodes and metastasise into the lungs with or without concurrent involvement of the intrathoracic lymph nodes (Brodey et al., 1983, Pereira et al., 2003). Epithelial tumours, such as carcinoma, readily metastasise via lymphatics to the regional lymph nodes (Sorenmo, 2003). We assume that sternal lymph node enlargement in the reviewed cases was caused by metastatic MGT. Pleural effusion noted in one dog was considered to be suspicious of intrathoracic metastatic disease.

Pleural effusion is often associated with pleural and mediastinal neoplasia, invasion of lymph nodes, obstruction or erosion of lymphatics or blood vessels, increased capillary permeability secondary to pleuritis and hypalbuminaemia (Mellanby, 2002). Differential diagnoses to be considered include chylothorax, hemothorax, pyothorax, pleural effusion due to hypoproteinemia, heart failure, diaphragmatic hernia, pancreatitis, pulmonary embolism and infarction, and idiopathic pleural effusion (Noone, 1985).

According to the literature carcinoma is the most common malignant MGT. Metastatic pulmonary involvement occur more frequently with sarcoma than with carcinoma (Brodey et al., 1983). Thoracic metastases are more common in dogs with inflammatory mammary carcinoma than with other tumour types (Perez Alenza et al., 2001). In all 5 dogs of our study with radiographic evidence of pulmonary metastases a mammary gland carcinoma was diagnosed histologically. The number of other types of malignant MGT in our study is too small to draw any conclusions about their tendency for metastasising to the lung.

Of the 136 dogs examined radiographically, 122 (89.7%) had no signs of intrathoracic metastatic disease. Overall, radiographic evidence of pulmonary metastases is low at the time MGT is diagnosed. Since all except one dog with established or suspected intrathoracic metastases were suffering from *malignant* MGT, histological characterisation of tumour malignancy is important for the correct work up of patients with MGT.

Our limited data suggest that a large portion of dogs with small pulmonary metastases may go undetected. While pulmonary nodules visible on radiographs are indicative of metastatic disease, normal pulmonary radiographs are inconclusive. Perception of metastases is limited by their size. Therefore, the number of pulmonary metastases in the lung is usually underestimated. The use of tomographic imaging (CT, MRI) to detect pulmonary metastases has been suggested as an alternative (Munden et al., 1997). Both modalities are not readily available and MRI is much more expensive. They also require anaesthesia and are therefore not practical screening methods.

In conclusion, in dogs with MGT thoracic radiographs provide limited information on the presence of pulmonary metastases and may therefore be restricted to dogs with histologically proven malignant MGT. Even then the majority of pulmonary metastases will be missed. Thoracic radiographs prior to anaesthesia and surgery may, however, be beneficial for detecting intrathoracic disease unrelated to MGT such as cardiac, pulmonary, pleural or diaphragmatic disease.

Symptômes métastatiques sur les clichés radiographiques thoraciques de chiens souffrant de tumeurs mammaires: une étude rétrospective (1990–1998)

Les tumeurs mammaires de 136 chiens étaient des tumeurs malignes pour 71% et des tumeurs bénignes pour 29%. On a diagnostiqué ou supposé à l'examen radiologique des métastases intratohoracales chez 13% des chiens souffrant de tumeurs malignes et 2,5% des chiens atteint de tumeurs bénignes. Six chiens atteints de tumeurs mammaires malignes ont été autopsiés, 5 présentaient des métastases pulmonaires, mais chez un seul on constatait radiologiquement des métastases intrathoracales. On peut en conclure que l'examen radiologique présente une faible sensibilité pour la détection de métastases intrathoracales en cas de tumeurs mammaires malignes.

Segni di malattie tumorali sulla radiografia toracica nei cani sofferenti di tumori della ghiandola mammaria: uno studio retrospettivo (1990–1998)

Tumori mammari (TM) in 136 cani erano maligni per il 71% e benigni nel 20% dei casi. Sono stati diagnosticate o presunte metastasi intratoraciche tramite esame radiologico nel 13.5% dei cani con TM maligno e nel 2.5% con TM benigno. Sei cani con TM maligno sono stati sezionati. In 5 sono stati riscontrati metastasi ai polmoni ma solo in un caso sono state individuate tramite esame radiologico intratoracico. Concludiamo che l'esame radiologico presenta una scarsa sensibilità per identificare metastasi intratoraciche nei casi di TM maligni.

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