

RESEARCH ARTICLE



Spontaneous tumors in dog as a model for comparative oncology

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Abstract

Pet animals are a very important resource and a valuable tool to tumor studies because of they live their biological life, and they live in the same ambient as human do. On the other hand, dog malignant mammary tumors are very common in middle-aged animals and they are similar model with breast human cancer. These tumors are appropriate and valid models to study cell cancer biology as well as to test new therapeutic drugs against cancer so long as dog develop spontaneous tumors with biological and histopathological features similar to it occur in human. Dog may be an attractive model to study hormone dependence of cancer. Tumors with probable relation to human cancer biology include mammary carcinoma, skin melanoma, oral squamous cell carcinoma, soft tissues carcinoma, etc. Skin tumors, especially skin melanomas are malignant tumor more common of dog. Metastasis is frequent and their relative resistance to chemo and radiotherapy make it an interesting model to study. Squamous cell carcinoma is an excellent model for radiotherapy studding. Skin tumors and soft tissues sarcoma are very good models for combined studding as chirurgical way with chemotherapy or with biological response modifiers. The aim of this study was to put in evidence that skin and mammary malignant tumors of dog may be used as an excellent model for comparative oncology.

Keywords: breast cancer, human, tumors, dog, oncology

1. Introduction

Dog and cat, as pet animals, develop spontaneous tumors, especially in skin and mammary glands. Their biological behavior and histopathologic features are similar to tumors that develop in humans [3,4,7]. These naturally tumors in pets are an interesting and important model tumor system available for studying human cancer biology and to test cancer therapeutic drugs [7, 8, 14]. Among canine tumors, they of mammary gland are one of the most common malignant tumors in this specie and they are considered as natural animal model of human breast cancer. The most important tumors with regard to human cancer biology include mammary carcinoma, soft tissue sarcomas, adenocarcinoma of skin, etc [1, 6, 8]. Canine malignant mammary and skin tumors are common in middle-aged animals [7]. Mammary gland tumors have a metastatic pattern similar to that in women, primarily to regional lymph nodes and skin. Canine mammary carcinoma is one of the most malignant tumors of mammary gland with a high rate of metastasis after surgical intervention, especially in skin. The aim of this study was to put in evidence that canine mammary malignant tumors and skin may be used as an excellent model for comparative oncology.

2. Material and Methods

The study was carried out at the Laboratory of Histopathology, Faculty of Veterinary Medicine and Safety Food and Veterinary Institute (SFVI), Tirana, Albania. In the present study, 41 cases of canine mammary tumors (CMT) were examined (29 malignant and 12 benign) and 10 cases of malignant skin tumors (MCST). Two of them were of metastatic nature, originated from mammary gland. The gross appearance of each tumor mass was recorded. Metastatic cases were from a bitch (unsterilized), 15 kg weight, 13 old years, mixed breed, in a good condition. It was presented at a Private Veterinary Clinic because of some nodules presented in mammary gland and skin areas. This animal was operated form a mammary gland tumor of forth couple of breast two years

earlier. It was diagnosed with a carcinoma of mammary gland. Two masses were presented in skin of head area (0.4 mm) and thoracic area (1 cm in diameter). Mammary and skin nodules were painless in palpation, with a solid structure and without ulcerations. The second case was of a Siberian Husky female dog, (sterilized), of five years old. Biopsied tissues were processed. Pieces of tumor tissues collected after biopsy were kept in jars containing neutral formaline saline solution for histopathological examination. Fixed material was transferred to a series of alcohol, and benzene, for the dehydration of the samples. After that, they are transferred in paraffin and then the material was cutting, in thickness of 5 μm and stained by Haematoxylin and Eosin and Masson-Trichrome methods, according to the procedure described by Lillie [5]. Then we made the observation on MOTIC, BA 210 microscope. CMT and MCST cases were of grade I and II grade. Tumors containing connective tissue invasion suggested bad prognosis.

3. Results and Discussion

Dog and cat, as domestic pets, are particularly valid models in studying of different diseases because of the same environment and life-style risks as human. Canine mammary tumors (CMT) and canine skin tumors (CST) are the most common neoplasms in the dog (prevalence of CMT - 0.2%). Histologically, approximately 50% of these neoplasms are diagnosed as malignant and distant metastases are common causes of death in these patients [10, 11]. Dogs age much faster than people, meaning canine cancers and treatment outcomes may be observed in much less time [14]. Spontaneous tumors that develop in dog share many characteristics with human cancers, such as histological appearance, tumor genetics, biological behavior, and therapeutic response, Michael Kastan said [2]. They also exhibit metastasis, similar to human breast cancers [12]. Mammary gland carcinoma metastases were found in a female dog with a good body condition. The animal had multiple nodular masses, present in the skin of the mammal, neck and thoracic region. It was operated by tumor masses in the 4th mammary couple and was diagnosed with breast gland carcinoma. The morphologic characteristics of cutaneous metastases (CM) correspond to the primary tumor. CM derived from cancer are relatively unknown in clinical veterinary practice, but they are important to be studied. CM presented 1% - 5% of cutaneous lesions in dog [10]. A big problem in veterinary oncology is a correct prognosis to post-surgical mammary cancer cases. In human breast cancer and in canine mammary tumor, histological type, histological grade and lymph node involvement are standard prognostic features [2, 12, 14]. In clinical examination, mammary lesions size were 0,3 mm – 2,1cm in diameter (fig. 1 and 2).



Figure 1. CMT in mammary region (2 years ago)

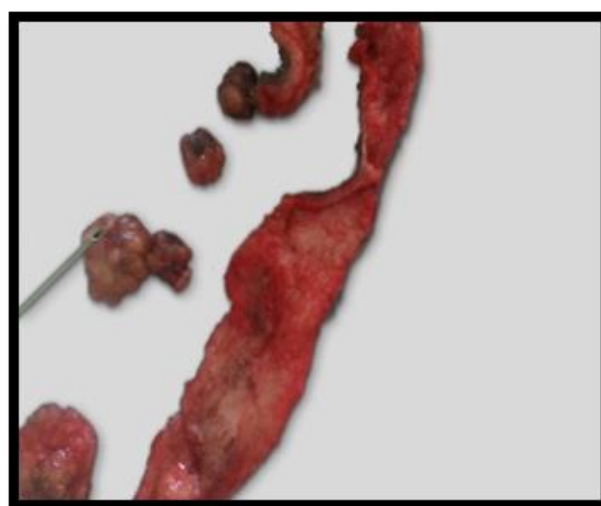


Figure 2. Biopsied masses of mammary gland



Figure 3. Metastatic lesion in head region



Figure 4. Metastatic lesion in thoracic region

Cutaneous masses varied from 0,4 mm -1cm in diameter (fig. 3 and 4). All findings were painless, aroused on skin, in round form, in brown to reddish color, with a solid consistence and without ulcerations. Malignant neoplasms are classified according to the histological degree of their development, like as differentiated gradients (G1), moderate differentiation (G2) and low differentiation (G3). Second-grade mammary carcinoma (G2) is characterized by proliferation of eosinophilic cytoplasm cells, with nuclei like as a vesicular structure (fig. 5). The cells are organized into islands and create intercellular bridges between them. It shows the added amount of deposited collagen, colored in blue, evidenced by dyeing with Masson Trichrome method (fig. 6).

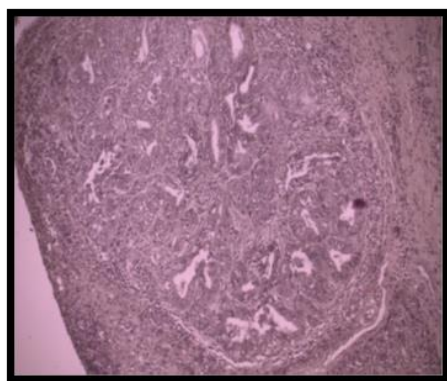


Figure 5. Microscopic findings of adenocarcinoma, G2.

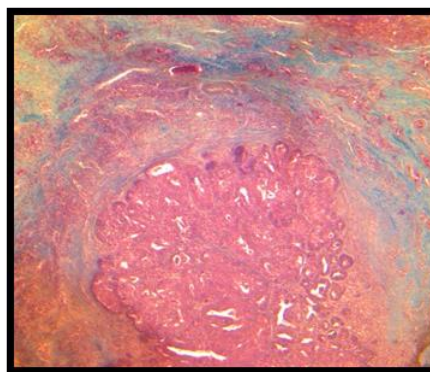


Figure 6. Microscopic findings of H-E, (X20) adenocarcinoma, G2. H-E, (X20)

Histopathological evaluation of breast and skin masses confirmed breast carcinoma and cutaneous metastases originated from mammary gland.

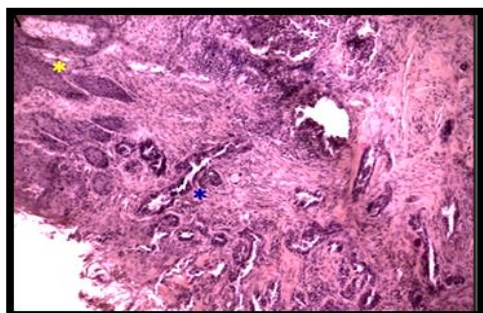


Figure 7. A lot of neoplastic cells around blood vessels (blue asterisks). H-E. (X10)

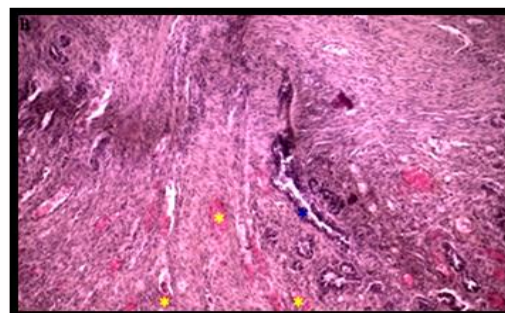


Figure 8. Newly blood vessels (yellow asterisks). H-E. (X10)

The histopathological features show the metastatic nature of skin CM of the breast origin. The metastases are characterized by diffuse infiltration of cells near blood vessels and those new being formed (angiogenesis) (fig. 7 and 8). Neoplastic cells have irregular borders, enlarged mitochondria and thick microfilament bundles, what it means their epithelial origin. Based on these histological characteristics, we find skin tumor represents cutaneous metastases (CM) of a primary tumor in the mammary gland. The morphological patterns of cutaneous metastases corresponded with the primary tumor.

Sarcoma is one of the most aggressive tumors, with a high metastatic potential. Metastatic disease is the most common cause of animal death while skin metastases are rare in animals. Skin metastases from a sarcoma were found in a Siberian Husky dog, of female sex (sterilized), 5 years old (fig. 9). The histopathologic interpretation of sarcoma-derived metastatic disorders determined the overall tumor architecture. In the skin are seen cell pleomorphisms and multiple mitosis, as well as epithelial cells located in the dermis layer. The central area of the cutaneous lesion manifests pleomorphism, some atypical mitosis and discrete fibroplasia is observed (fig. 10).

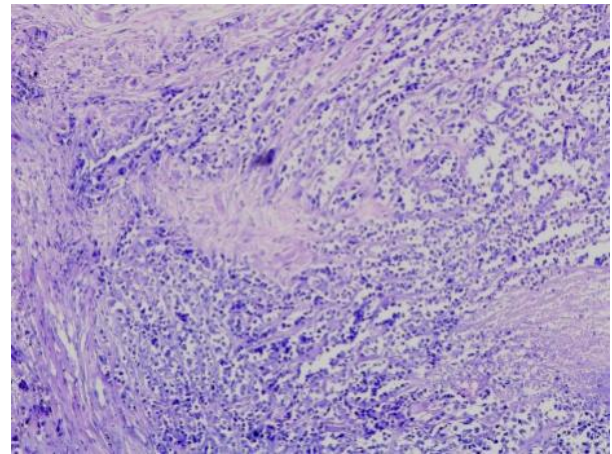


Figure 9. Macroscopic finding of CM sarcoma, Siberian husky **Figure 10.** Microscopic findings of CM originated by of a sarcoma. H-E. (X10)

Lastly, there has been renewed interest in comparative oncology, the study of spontaneously developing cancers in animals as models for human ones, provide important opportunities to expand our understanding of cancer biology and to develop new therapies [2, 8, 15].

4. Conclusions

Mammary gland and skin biopsy findings are significant in diagnose of neoplasm and its metastases. The morphological, cytological and histological patterns of CM corresponded with the primary mammary gland tumor. Their evaluation helped to put together features of primary and secondary (metastatic) tumors. Histopathological method of tumour diagnose has to be used for.

CMs are a small but very important part in veterinary oncology, because of their importance in knowledge of these findings in human oncology.

This paper will modestly help to understand tumor type and its metastasis as model for human cancer biology.

5. References

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