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The Hidden Danger: Canine Mammary Tumour

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Abstract

The most common neoplasia in female dogs is a mammary tumour, which typically manifests between the ages of 9 and 11. The posterior mammary glands are more commonly affected than the anterior glands, and they might manifest as a single or multiple nodules. Dogs can develop benign as well as malignant tumours; based on histological criteria, around half of the tumours are malignant. A broad spectrum of pathogenic characteristics and clinical signs can be seen in mammary gland tumours. A variety of hormones and growth factors are important in the formation of this tumour, but research is still ongoing to determine how they affect tumour growth and if they have any predictive significance. There is a hormonal component to their growth; Oestrogen and progesterone receptors have been identified in 50% of malignant and 70% of benign mammary gland tumours. Also, compared to tumours that express the receptors, those lacking hormone receptors are less differentiated and more aggressive. Complete surgical excision is the preferred course of therapy for mammary gland tumours, and all removed masses should be sent for histologic analysis. Dogs may acquire cancer on their own and also have many biological, clinical, pathological, and molecular traits similar to human cancer diagnoses. In both species, mammary tumours rank among the primary causes of mortality. Mammary tumour incidence varies widely and is influenced by biological, pathological, cultural, and socioeconomic variables, such as breed, advanced age, obesity, hormonal condition, and food. Although several attempts have been undertaken to create a genetic categorisation of canine mammary tumours in order to expand the range of treatment options, which currently mostly rely on surgical tumour removal, then diagnosis is primarily based on histology.

Keywords: Mammary Gland, Tumours, Treatment, Diagnosis, Cytology, Histopathology

Introduction

Cancer is a broad category of diseases characterized by the uncontrolled proliferation of abnormal cells that have the potential to invade nearby tissues. The mammary gland is an altered form of the apocrine sweat gland, with ducts and alveoli encircled by arteries, nerves, and connective tissue. Usually, five pairs of mammary glands are found in dogs: two thoracic, two abdominal, and one inguinal. The mammary gland tumours in dogs are of two types, namely, Benign and Malignant. Malignant tumours are locally invasive, anchored to deep tissues or the skin above them, may be ulcerated and haemorrhagic and develop quickly in contrast to benign tumours, which are often tiny, well-circumscribed, firm to the touch, and grow slowly. Although the brain, bones, and abdominal organs can also be affected as well, the lungs and regional lymph nodes are frequently the locations of metastases. It is also among the leading causes of mortality in both canines and humans. In dogs, 4 million new cases of cancer are diagnosed annually; in humans, the number of cancer-related deaths is around 10 million, and there are 19.3 million new cases diagnosed. For dogs older than ten years old, cancer is the leading cause of mortality; 50% of these animals have

cancer, and one in four of them pass out due to it. Dogs with tumours are used for research purposes for creating novel medications or treatments, as well as for clinical trials.

Factors Affecting Canine Mammary Tumour

1. **Genetic Factor**: Genetic changes impact the development of breast tumours, and certain breeds seem to be more cancer-prone than others. Studies on the incidence of breast tumours by breed differ from one another. German shepherds, Indian spitz dogs, Rottweilers, and Labradors are among the breeds most likely to acquire breast cancer in India. Numerous genes have been investigated to determine the extent to which genetic factors may predispose to canine mammary tumours. For example, a transmembrane protein known as Epidermal Growth Factor Receptor 2 (EGFR-2 or HER-2) that typically controls cell proliferation is encoded by a proto-oncogene. On the other hand, when HER-2 is mutated, the cells experience neoplastic alterations. The presence of HER-2 mutations and overexpression has been seen in both benign and malignant CMT. p53 is an additional gene implicated in the development of breast tumours. Mutations in the p53 tumour suppressor gene contribute to the carcinogenic process in several organs, including the mammary gland. This gene produces a protein that normally governs the cell cycle and programmed cell death. There is another tumour suppressor gene known as Breast Cancer 1 (BRCA1) that has been linked to both human and canine breast cancer. Because BRCA1 is a nuclear protein, its lack of function may cause an aberrant distribution of the cytoplasm. The lack of nuclear BRCA1 expression in the bitch is linked to malignant features of the tumours, such as a high proliferation index and minimal ERα expression, indicating that it contributes to the malignant nature of this tumour.
2. **Sex**: Males and females are both affected by tumours. However, the canine mammary tumour was found mostly in females.
3. **Age:** Higher incidence was found after the sixth year of age, with the maximum being 9 to 11 years.
4. **Spaying status:** The most significant decrease in incidence was found in Dogs spayed before their first oestrus and between the first and second oestrus. Advanced age at the time of spaying increases the incidence of tumours, and no positive effect of spaying was found after the fourth oestrus.

Histological And Molecular Classification

The morphology of canine mammary tumours varies greatly, and they are typically made up of many cell types, either alone or in combination, such as mesenchymal, myoepithelial, and luminal epithelial cells. Some have a mixture of epithelium and myoepithelial tissue, such as benign mixed tumours or carcinosarcoma. They can be of epithelial origin or of mesenchymal. Numerous criteria are involved in the diagnosis of malignant breast cancers, such as the tumour type, mitotic index, nuclear and cellular pleomorphism, presence of necrotic areas, lymphatic and peritumoural invasion, and regional metastatic lymph node. Anaplasia, tubule development, mitotic activity, and nuclear pleomorphism are all quantified as part of the histological grading system for canine mammary tumours. There are five molecular subtypes of mammary gland tumours: luminal A, luminal B, Luminal B HER-2+ (epidermal growth factor 2 positive), HER-2, triple-negative, and HER-2 (epidermal growth

factor 2 negative). This makes it possible to choose a particular targeted therapy, such as anti-estrogen medications for the luminal A subtype. Thirty to thirty-five per cent of canine mammary tumours express HER-2, which is also regarded as a significant tumour marker.

Mammary tumours are usually firm, well defined lumps that can vary in size from m illimetres to centimetres. They might appear in many glands simultaneously and have varying histological grades and kinds. In a single mammary gland, many cancers may occur simultaneously. The most affected mammary gland is the caudal abdominal (up to 60% of cases). There may be traumatisation or ulceration of the skin in the afflicted region. Assessing and examining the lymph nodes in the area is essential for making a diagnosis. At the time of diagnosis, the majority of dogs with mammary tumours are clinically healthy. On the other hand, metastatic patients may have oedema, lameness, coughing, dyspnea, weariness, and weight loss. The clinical symptoms depend on the site and degree of metastasis. There is variation in lymph node involvement, and it can encourage distant metastasis, usually to the lung.

Diagnosis

1. **Accidental finding**: A mammary tumour is frequently diagnosed acci dentally during a physical examination or when a p atient visits the veterinarian because animals have one or more mammary gland nodules. Histological analysis is used to determine the final diagnosis and to find the tumour grade
2. **Biopsy**: For a histopathological diagnosis of the tumour, an excisional biopsy is a desirable choice since it permits a thorough histological study. It is important to analyse each tumour separately if the patient has more than one, as various kinds of cancers can coexist in the same patient.
3. **Fine Needle Aspiration Cytology (FNAC):** The inconsistency of cell shape in distinct tumour sites and the variety of canine tumours are the main reasons why FNAC does not always result in a diagnosis. As a result, it is frequently impossible to distinguish between benign and malignant tumours of epithelial origin. Cytology can be useful to rule out differential diagnoses such as mastitis, lipomas, mast cell tumours and others.
4. **Histopathology**: The tumour type, histological grade of malignancy, presence of vascular or lymphatic permeation, surgical margins, lymph node status, and tumour size are all revealed by a histopathological diagnosis. For canines with mammary tumours, this information together with the stage aids in determining the prognosis.

Since the lungs are the most common location for metastases of mammary tumours, radiographic scans of the chest are crucial for determining if metastases have spread to the lungs. The liver, bone, brain, spleen, kidney, adrenal gland, uterine, heart, muscle, and pancreas are some less common places where metastases can occur. To evaluate these potential situations, further investigations such as CT scans, X-rays of the bones, and abdominal ultrasonography are required.

Treatment

Surgery is the primary course of treatment for mammary tumours in dogs, with the exception of inflammatory carcinoma, which is better treated with chemotherapy and palliative care. The tumour's size, position, and the existence of lymphatic outflow from the afflicted mammary gland determine whether surgery is necessary or not. It has been observed that 60% of patients have several mammary tumours, each of which behaves as a separate primary tumour with distinct histological

features. Malignant tumours are also substantially bigger than benign ones. Surgery aims to remove every tumour with complete surgical margins and/or stop the development of additional tumours in the mammary gland . Surgery alone is not a successful treatment for canines with unfavourable clinical or histological prognostic markers, and they have an increased risk of developing new mammary tumours.

The ability to examine the tissue histopathologically is another advantage of surgically excising breast tumours. As a result, it has been linked to longer survival times and improved outcomes for patients.. Surgery includes simple mastectomy, regional mastectomy, radical mastectomy, or a combination of these techniques, depending on the size, location, and number of the tumours. Large tumours, lymph node metastases, or poor histological features typically do not respond well to local therapy; instead, patients need systemic treatment, such as hormone therapy or chemotherapy.

It is thought that the lymphatic system serves as the primary pathway for canine mammary cancer metastases. This is one of the causes for the surgical excision of the breast tumour, which also involves the removal of the lymph node and the glands connected to lymphatic drainage.

Discussion

Globally, mammary tumours are the primary cause of cancer-related mortality in female dogs. Surgery is the primary therapeutic approach for canine mammary tumours. A few studies focused on the use of doxorubicin, carboplatin, cyclophosphamide, 5-fluorouracil, mitoxantrone, and docetaxel in dogs undergoing chemotherapy, with varying degrees of success and toxicity. There is a lack of standardisation in the selection and use of chemotherapy type criteria. Due to their tendency to produce spontaneous mammary tumours that closely resemble human breast cancers, dogs provide excellent models for studying comparative oncology. Canine mammary carcinoma shares many molecular characteristics with human mammary carcinoma, such as variable ER expression status, cyclooxygenase overexpression, p53 mutations, and features of the tumour microenvironment, such as the presence and function of cancer-associated fibroblast, macrophages, and T-lymphocytes. Dogs have a short lifespan, which makes it possible to evaluate therapy responses and get clinical test findings more quickly. It is simpler to carry out procedures in dogs than in mouse models, including as sample collection, surgery, and histology. These procedures are often carried out in human medicine. Canines are a desirable animal model for studying the carcinogenesis of breast cancer because of all of these factors.

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