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FELINE MAMMARY NEOPLASIA: CLINICAL AND PATHOLOGICAL FINDINGS, AND INVESTIGATION OF METASTASIS AND MICROMETASTASIS IN SENTINEL LYMPH NODE

NEOPLASIA MAMÁRIA FELINA: ACHADOS CLÍNICOS E PATOLÓGICOS E INVESTIGAÇÃO DE METÁSTASES E MICROMETÁSTASES EM LINFONODO SENTINELA

NEOPLASIA MAMA FELINA: HALLAZGOS CLÍNICOS, PATOLÓGICOS E INVESTIGACIÓN DE METÁSTASIS Y MICROMETASTAS EN EL NÓDULO LINFÁTICO CENTINELA

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ABSTRACT:

Objectives: This study aimed at evaluating clinical and histopathological aspects in sentinel lymph nodes, as well as the presence of metastasis and micrometastasis. Methods: 28 female cats aged between five and 17 years were selected, in which thoracic radiography, abdominal ultrasonography, hemogram, serum biochemistry, and cytology were performed for tumor staging and preoperative evaluation. Blue vital dye was used to locate the axillary lymph node, after which mastectomy and lymphadenectomy were performed. Results: according to the tumor-node-metastasis system, 64.28% of patients were classified as stage 3, 21.43% as stage 1, and 14.28% as stage 2. The most affected breasts were the inguinal (34.78%), followed by the caudal abdominal (32.61%), the cranial abdominal (21.74%) and the thoracic (10.87%). 80.47% of neoplasms were classified as malignant carcinomas. Metastasis was found in 21.43% of inguinal lymph nodes and was not observed on axillary lymph nodes. Conclusions and relevance: evaluation of mammary neoplasms, including the clinical staging of the disease, contributes to the therapeutic approach by enabling the delineation of a more accurate diagnosis and prognosis, and a more appropriate treatment. Moreover, lymphadenectomy of axillary lymph nodes was difficult to perform even after using the vital dye to map and locate them.

KEYWORDS: Breast; mastectomy; tumors.

RESUMO:

Objetivos: Este estudo teve como objetivo avaliar aspectos clínicos e histopatológicos em linfonodos sentinela, bem como a presença de metástases e micrometástases. Métodos: Foram selecionadas 28 gatas com idade entre cinco e 17 anos, nas quais foram realizados radiografia torácica, ultrassonografia abdominal, hemograma, bioquímica sérica e citologia para estadiamento tumoral e avaliação pré-operatória. O corante azul patente foi utilizado para localizar o linfonodo axilar e após foram realizadas mastectomia e linfadenectomia. Resultados: de acordo com o sistema tumor-nódulo-metástase, 64,28% das pacientes foram classificadas como estágio 3, 21,43% como estágio 1 e 14,28% como estágio 2. As mamas mais acometidas foram a inguinal (34,78%), seguida pela abdominal caudal (32,61%), abdominal cranial (21,74%) e torácica (10,87%). 80,47% das neoplasias foram classificadas como carcinomas malignos. Metástase foi encontrada em 21,43% dos linfonodos inguinais e não foi observada em linfonodos axilares. Conclusões e relevância: a avaliação das neoplasias mamárias, incluindo o

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estadiamento clínico da doença, contribui para a abordagem terapêutica ao possibilitar o delineamento de diagnóstico e prognóstico mais precisos, e um tratamento mais adequado. Além disso, a linfadenectomia dos linfonodos axilares era difícil de ser realizada, mesmo após o uso do corante azul patente para mapeá-los e localizá-los..

PALAVRAS CHAVE: Mama; mastectomia; tumores.

DESAFIOS

RESUMEN:

Objetivos: Este estudio tuvo como objetivo evaluar aspectos clínicos e histopatológicos en el ganglio centinela, así como la presencia de metástasis y micrometástasis. Métodos: Se seleccionaron 28 gatos con edades comprendidas entre cinco y 17 años, a quienes se les realizó radiografía de tórax, ecografía abdominal, hemograma, bioquímica sérica y citología para la estadificación del tumor y evaluación preoperatoria. Se utilizó tinte azul patente para localizar el ganglio linfático axilar y luego se realizó mastectomía y linfadenectomía. Resultados: según el sistema tumor-nódulo-metástasis, el 64,28% de las pacientes se clasificaron en estadio 3, el 21,43% en estadio 1 y el 14,28% en estadio 2. Las mamas más afectadas fueron la inguinal (34,78%), seguida de el abdominal caudal (32,61%), abdominal craneal (21,74%) y torácico (10,87%). El 80,47% de las neoplasias fueron catalogadas como carcinomas malignos. Se encontraron metástasis en el 21,43% de los ganglios linfáticos inguinales y no se observaron en los ganglios linfáticos axilares. Conclusiones y relevancia: la evaluación de las neoplasias mamarias, incluyendo la estadificación clínica de la enfermedad, contribuye al abordaje terapéutico al permitir diseñar un diagnóstico y pronóstico más preciso, y un tratamiento más adecuado. Además, la linfadenectomía de los ganglios linfáticos axilares fue difícil de realizar, incluso después de utilizar tinte azul patente para mapearlos y localizarlos.

Palabras clave: Mama; mastectomía; tumores.

INTRODUCTION

Mammary neoplasia in domestic female cats represents 17% of all tumors in the species. With a malignancy rate between 80% and 90%, more than 80% of cases are diagnosed as carcinomas. This type of tumor shows an invasive behavior and metastatic potential, and the prognosis ranges from guarded to unfavorable (Padilha 2020).

Clinical staging is important for evaluating the primary tumor and regional lymph nodes, identifying metastasis in other organs, and determining the most appropriate therapeutic approach for each case. Furthermore, it enables the description of cancer aspects, such as location, dissemination, and effects on other organs and their functions (Chiti et al., 2021).

Female cats with mammary carcinomas usually show an overall good health status and, in most cases, the neoplasia is at an advanced stage with chance of metastasis. Indeed, metastasis in lymph nodes is one of the most important prognostic factors for the survival in animals and evaluating regional lymph nodes is essential for breast cancer staging. One of the challenges for staging

is the inability to visualize the sentinel lymph node, resulting in failures that may lead to a lower quality treatment or to axillary recurrence (Cassali, 2020; Hass et al., 2023).

Considering the high morbidity, aggressive behavior and fast evolution, this study aims at evaluating the clinical and histopathological aspects of female cats with mammary neoplasia, as well as searching for metastasis and micrometastasis in sentinel lymph nodes.

METHODOLOGY

This study was conducted after receiving approval from the Ethics Commission on Animal Use (CEUA) from Universidade Federal Rural de Pernambuco (UFRPE) under the license no 113/2017.

A total of 28 female cats from different breeds and ages were assessed, brought from the oncology ambulatory service of the Veterinary Hospital (HOVET) of the Department of Veterinary Medicine (DVM) at UFRPE. Patients with neoplasia in the mammary chain and absence of distant metastasis were included. All animals underwent a clinical examination and were catalogued in individual files, which included data related to anamnesis and records of physical and supplementary exams.

During anamnesis, questions were made regarding dietary and behavioral habits, time of nodule development, use of contraceptive methods, whether the animal was spayed and whether it had undergone a surgical procedure related to mammary neoplasms.

Parameters observed during physical examination included temperature, eye and gum mucosae, as well as lymph node palpation. Breasts were evaluated individually by observing the presence of nodes, coloration, adherence, ulceration, and secretion. Signs of inflammation such as pain, redness and erythema were also evaluated. The size of each node present in the mammary chain was measured with a pachymeter.

The body condition score (BCS) was based on the inspection and palpation of the patients, using a numerical scale (1-9) to reduce subjectivity of intermediate values, according to Laflamme.

As suggested in the protocol by the World Health Organization (WHO), staging was conducted in all patients according to the Tumor-Node-Metastasis (TNM) system.

After results from both the physical and the supplementary exams were evaluated, animals considered fit for anesthetic surgical procedures were subject to a bilateral mastectomy, lymphadenectomy and ovariohysterectomy (OVH), when necessary, following Fossum (2008). For lymphatic mapping and locating axillary lymph nodes, 0.25ml of patent blue vital dye was injected via intradermal injection in the periareolar region of each cranial thoracic breast. Lymphadenectomy was performed no later than 30 minutes after injection, thus avoiding impregnation of other structures.

The excised material resulting from the mastectomy and lymphadenectomy was stored in 10% formalin, processed by impregnation in paraffin, sliced into 4µm-thick sections and stained in hematoxylin and eosin for evaluation under an optical microscope. Histological sections were morphologically classified according to Cassali (2014). Histological grading was performed in the Animal Pathology Laboratory of UFRPE following the TNM system proposed by Owen (1980).

Data analyses were carried out through inferential statistics based on categories of age group, tumor stage, body score, type of tumor – benign/malign, spayed/unspayed, as well as periods of biological material collection.

RESULTS AND DISCUSSION

The 28 female cats with mammary neoplasia assisted at HOVET/UFRPE ranged between five and 17 years old (average of 10.29 years). Those aged less than seven years were considered 'young', from eight to 10 years were considered 'adults', and those older than 10 years were considered 'seniors'. Senior cats showed the highest incidence (46.43%, n=13/28) of alterations in the mammary gland.

Out of the 28 animals analyzed in this study, 46.43% (n=13/28) were spayed, 89.29% (n=25/28) had no defined breed and 10.71% (n=3/28) were Siamese. Regarding the use of contraceptives, 67.86% (n=15/28) of analyzed individuals underwent hormonal contraceptive treatment at some point during their lives.

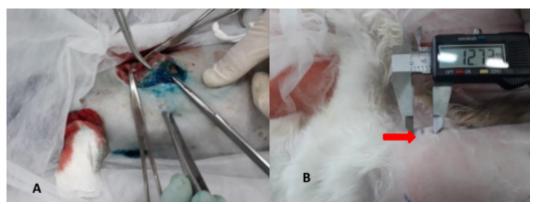
As for dietary habits, 60.61% (n=17/28) of patients with mammary neoplasia were fed only commercial pet food, while 35.71% (n=10/28) were fed exclusively homemade food, and 3.57% (n=1/28) were fed a mix between the two. The type of commercial pet food offered to the animals was not evaluated.

For all animals, cytological examinations were performed through puncture by fine needle aspiration. However, when comparing the results from this exam to that of the histopathological exam, a difference was observed in 21.43%

(n=6/28) of the clinical reports. In total, 46 mammary glands affected by neoplasia were recorded. Out of these, the less frequent were thoracic glands, representing only 10.87% (n=5/46), followed by cranial abdominal with 21.74% (n=10/46), caudal abdominal with 32.61% (n=15/46), and inguinal glands with 34.78% (n=16/46). It should be noted that while no metastasis was observed in axillary lymph nodes, 21.43% (n=6/28) of patients presented metastasis in inguinal lymph nodes.

Despite the use of patent blue vital dye (Fig. 1) in all patients, identification and removal of the axillary lymph node could only be performed in one animal (3.57%). Regarding nodule size, 34.78% (n=16/46) had less than 2 cm in diameter, 21.74% (n=10/46) measured between 2 and 3 cm, and 43.48% (n=20/46) were larger than 3 cm. Tumor size is an important parameter to evaluate the clinical stage of the disease, as well as node status. Metastasis in the lymph node was observed in 25% (n=5/20) of tumors larger than 3 cm, in 10% (n=1/10) of tumors between 2 and 3 cm, and was not observed in tumors with less than 2 cm.

Figure 1 (a)- Location and dissection of axillary lymph node. (b) – Reactive axillary lymph node.



Fonte: Arquivo pessoal, 2017.

Ulceration was present in 56.52% (n=26/46) of neoplasms, which was likely due to the tumor size and evolution time. In neoplasms under 2 cm in diameter, ulceration was observed in 30.75% (n=8/26) cases. Out of these, 50% (n=4/8) had an evolution time of one to five months, while the other 50% (n=4/8) showed an evolution time from six to 12 months. For neoplasms measuring between 2 and 3 cm, 23.7% (n=6/26) had ulcerations, out of which 50% (n=3/6) had an evolution time of up to 1 month, 33.33% (n=2/6) from one to five months, and 16.67% (n=1/6) from six to 12 months. Lastly, ulceration was present in 46.15% (n=12/26) of tumors larger than 3 cm in diameter, out of which 8.34% (n=1/12) showed an evolution time of up to one month, 33.33% (n=4/12) from one to five months, and 58.33% (n=7/12) from six to 12 months.

Malignant neoplasms were found in 80.47% (n=37/46) of the mammary glands analyzed. Through histological examination, 32.43% (n=12/37) were classified as grade II tubular carcinoma, 29.73% (n=11/28) as grade II cribriform carcinoma, 16.23% (n=6/37) as grade II solid carcinoma, 10.87% as grade I cribriform carcinoma, 5.40% (n=2/37) as grade I tubular carcinoma, and 2.70% (n=1/37) as grade II papillary carcinoma. Among benign neoplasms (19.57%, n=9/46), 88.89% (n=8/9) of cases were classified as fibroadenomas and 11.11% (n=1/9) as adenomas. Only one animal showed two histological types on the same breast (2.17%), both of which were malignant.

For body score evaluation, animals were classified as underweight, ideal weight and overweight, which represented 28.57% (n=8/28), 42.86% (n=12/28) and 28.57% (n=8/28) of cases, respectively. Cachexia was observed in 28.57% (n=8/28) of patients, although this finding was prevalent in a small number of animals in this study. Among the female cats with this disorder, 87.5% (n=7/8) showed malignant neoplasia and were staged at TNM 3. Out of those, 62.5% (n=5/7) were seniors and 25% (n=2/7) were adults. Although cachexia is associated with advanced stages of oncological disease in the literature, it should be noted that the tumor was benign in 12.5% (n=1/7) of the evaluated animals, presented no ulceration, and the animal was young.

The clinical staging of patients with mammary tumors was performed according to the system proposed by the WHO. Of the 28 cases analyzed in the present study, 21.43% (n=6/28) of patients were classified as Stage I, 14.8% (n=4/28) as Stage II, and 64.28% (n=18/28) as Stage III. Animals with distant metastasis were not included in this study, and thus no patients were classified as Stage IV.

The presence of mammary neoplasia in female cats with ages varying from nine months to 23 years was described by Price (2023). Although in the present study the age group was different from the aforementioned study, the disease was observed in young, adult and senior animals, with the latter representing the most affected group.

Breed was not a decisive factor for the appearance of mammary neoplasia in female cats, however Price (2023) reports that pure breed cats are more predisposed. Although the Siamese breed was present in the studied group, most animals with mammary neoplasia had no defined breed, which agrees with studies by Srisawat et al. (2024).

Spaying is defined as a preventive measure for the development of mammary neoplasms, if performed early. Despite the occurrence of neoplasia in spayed animals in the present study, it was noted that OVH was performed after the first year of the animal's life, highlighting what Oliveira (2020) reported, that the probability of breast carcinoma increases gradually with the age at which the animal was spayed (Srisawat et al., 2024; Price, 2023).

It is important to note that the use of synthetic progestogens influences tumor onset. As reported by (Fernandes et al., 2020), the longer the period during which the animal was exposed to this medication, the higher the risk of developing mammary tumors. In this study, most female cats underwent hormonal treatments and, even though this happened at different life stages, its effect was clear.

Costa (2020) highlight that dietary habits are an intrinsic cause of mammary tumor and, although state that homemade fat-rich diets can lead to the onset of neoplasia, the main source of nutrition in this study was commercial pet food, which represented the group most affected by mammary neoplasms.

Despite cytology providing valuable information for tumor characterization, six out of the 28 cases analyzed showed inconsistencies between cytologic and histopathological reports. According to Barros (2021), histopathological examination is the most effective means to obtain information on tumor histomorphology.

Epithelial tumors, such as the ones found in the evaluated patients, usually spread via the lymphatic system, and the most common sites are regional lymph nodes, lungs and liver (Petrucci et al., 2020). The lymphatic system is considered the most common route for metastasis. However, it is important to evaluate sentinel lymph nodes even if there are no alterations during physical examination. Lymph node status acts as a prognostic factor in breast tumors, and it is of great value for determining the therapeutic approach Granados-Soler et al. (2020).

Because of the axillary lymph node's location in the armpit together with arteries, veins and nerves, it is rarely evaluated due to potential morbidity (Andrade, 2017). Indeed, it is evaluated only when palpable, as occurred in one of the patients of the present study, in which the lymph node was swollen at the time of palpation, thus facilitating its identification (figure 1b). Andrade (2017) highlight that one of the challenges in staging is the difficulty in visualizing the sentinel lymph node, resulting in failures that may lead to a poor-quality treatment or to the recurrence of neoplasia in the axillary lymph node.

The mammary glands located in the inguinal area are more predisposed for tumor development, and that is associated with the abundance of parenchyma in this region, the increasing numbers of local hormonal receptors, and the intense vascularization supplied by the caudal superficial epigastric artery and external pudendal artery branches. These are factors of great influence for the major involvement of inguinal lymph nodes (Andrade, 2017; Mendes, 2023), as observed in the patients of this research, in which only one patient had a reactive axillary lymph nodes. Corroborating with the literature, the patients had a higher incidence of mammary neoplasms in the caudal glands, of which the caudal abdominal glands represented 32.61% and the inguinal glands 34.78%, associated with the presence of metastasis in 21.43%. in inguinal lymph nodes.

Metastatic involvement of the inguinal lymph node is more common, since the axillary lymph node is especially responsible for the physiological lymphatic drainage of M1, M2 and M3, with breasts being less affected by breast neoplasms (Cassali, 2020), which is in agreement with the experiment in question. It is recommended that the histopathological evaluation of regional lymph nodes should be performed, regardless of the degree of malignancy of the neoplasm. It is necessary to surgically remove them together with the tumor, for subsequent analysis and evaluation of changes in the lymph node, such as metastasis or suspected infiltration (Santos et al., 2020), as occurred in the present study.

Tumor size is one of the most important clinical factors evaluated for the prognosis of mammary neoplasms in women, female dogs and cats (Estralioto e Conti, 2019), corroborating with the findings of the present study, since tumors larger than 3 cm showed the highest metastasis indices in lymph nodes when compared with smaller tumors.

The most common carcinoma types found in the studied patients were tubulopapillary, solid, and cribriform. This is in agreement with Silva et al. (2020), who cite mammary carcinomas and adenocarcinomas as the most common tumors found in female cats, representing more than 80% of neoplasms in the species. According to Srisawat et al. (2024), the histological type influences the patient's prognosis and therapeutic approach, and the excised material must be sent to histopathological examination.

Tumor mass can be simultaneously made up of benign and malignant areas, as well as more than one histological type. as observed in one of the patients of the present study. Multiple tumors are common in female cats, although there is a lower tendency for simultaneously showing benign lesions (Berselli, 2021).

Cachexia was a prevailing finding, even being found in a small number of animals in the study. This corroborates the findings, who reports that the frequency is higher in cats than in dogs with neoplasia. Although literature associates cachexia with advanced stages of oncological disease or with disorders of geriatric patients, it should be noted that this syndrome was also observed in a young animal with a benign tumor and no ulceration (Parra, 2024).

Staging of feline patients with mammary neoplasm was performed according to the criteria established by the who, which considers tumor size and presence of metastasis in regional lymph nodes or distant sites. In the present study, interpreting patients' clinical stages was fundamental for establishing a prognosis and the therapeutic approach to be applied, in agreement with Cassali (2020).

Conclusions

In the present study, mammary carcinoma was the most common tumor found in female cats, with a higher incidence in inguinal glands. Furthermore, most patients were staged at TNM 3. Lymphadenectomy of axillary lymph nodes was considered a difficult procedure, even after using vital dye for mapping the region. Therefore, the evaluation of mammary neoplasia and the search for metastasis and micrometastasis in sentinel lymph nodes of cats with mammary neoplasia helps the therapeutic approach by enabling more precise diagnosis and prognosis, which leads to a better treatment for the affected patients.

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Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

This work involved the use of experimental animals and the study therefore had ethical approval from an established committee as stated in the manuscript.

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