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Original Article:

Feline Mammary Carcinomas as a Model for Human Breast Cancer: A Case-series Study

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Abstract

Introduction: Feline mammary carcinoma (FMC) is the third most common cancer in cats. Diagnosis of mammary gland tumors (MGTs) increases every year; this might be due to the rise in occurrence or improvements in methods of detecting MGTs. Determinants associated withtheir occurrence are studied in the present paper.

Materials and Methods: In this case-series study, 40 queens with FMC were referred to the determined major veterinary hospitals of Tehran for treatment between 2020 and 2022; their mammary carcinoma had been confirmed by the attended pathologist. Different parameters including age of cancer diagnosis, breed, reproductive status, BCS, diet type, parity, tumor size, multiple tumors, ER and PR status, location and type of treatment were recorded on the day of presentation using a checklist.

Results: Domestic short hairs were overrepresented. Also, queens with old age (more than 9 years old), homemade diet, sexually intact status, no parity, obesity, ER and PR positivity had higher frequency towards developing FMC. Imbalanced homemade diet energy is a speculated cause.

Conclusion: Humans and their companion animals share the same environment, thus being exposed to the same environmental risks. Although canine mammary tumors have been the focus of human breast cancer (HBC) modeling, this study also aimed to compare current feline mammary carcinoma determinants with previously defined human breast cancer determinants to produce a model. Based on the results of this study, we concluded that FMCs are a proper model to study HBC.

Keywords: Determinants, FMC, Human mode, Tehran

1. Introduction

The occurrence of cancer ceaselessly increases worldwide among pets and humans. Due to the complexity of cancer biology, medical research lags behind despite the importance of this disease [1]. Companion animals have long been a part of human life [2]. Currently, cats are the most common pets in developed countries [3]. Since they share the same environment as their owners, alongside other biological, hormonal, and genetic similarities, they can be a proper model for human cancer [4, 5]. Feline mammary tumors (FMTs) are the third-most-common cancer in cats, accounting for 17% of all neoplasms and 25% of tumors in queens [6, 7]. Although cats are more popular than dogs, canine mammary tumors have been the focus of comparative oncology. This may be due to the fact that the full genome of dogs has been available since 2005, but cats' full genome has just recently been made accessible [8, 9]. Most of the FMTs are malignant (85-90%) [10], making FMTs the first cause of death in cats [4]. Thus,

early diagnosis is pivotal in the survival rate and the prognosis of FMC.

The incidence of FMTs is higher in middle-aged to old female cats (10-12 years old), with Siamese and domestic short-haired (DSH) as the most susceptible breeds [11, 12]. Although age plays an important predisposing role, the risk does not become significant until 7-9 years of age [10]. Also, it is noteworthy that Siamese cats are prone to many types of tumors, not just FMT, and this may be due to the germline alterations in cancer predisposing genes or a defection in genes repressing tumors [10]. FMTs are commonly diagnosed in intact females, while rarely observed in spayed females or males [13]. The expression of estrogen and progesterone receptor (ER and PR) along with hormonal therapy seems to affect the incidence of FMTs [14]. Performing ovariohysterectomy (OHE) before the age of six months is a proven protective factor in the prevention of FMTs, reducing the development in most cases (91%) [6, 14]. However, its effect reduces quickly over the first few years. Risk reduction of performing OHE before 6 months, 7-12 months, and 13-24 months drops 91%, 86%, and 11%, respectively. No significant effect was reported for performing OHE after 24 months of age [14].

There are also other factors that are less studied specifically in FMTs, including body condition score (BCS), diet type, and parity which were effective in other types of cancers [10]. Since there are no previous data regarding the determinants of FMCs in Iran, in this research we aimed to study these determinants in FMCs in Tehran metropolis over the years of 2020-2022 in cases referred to major hospitals of Tehran.

2. Materials and Methods

In this case-series study, 40 queens with FMC were referred to the determined major veterinary hospitals of Tehran for treatment between 2020 and 2022; their mammary carcinoma had been confirmed by the attended pathologist. Different parameters including age of cancer diagnosis, breed, reproductive status (intact, spayed), BCS, diet type (homemade or commercial), parity (number of litters), tumor size, having multiple tumors, location of mammary tumors, and type of treatment use were recorded using a checklist. BCS was assessed on a 3-point scale (1-3), attributed as lean, normal, and obese, respectively. Data on pet management practices were also collected and recorded. Immunohistochemistry was used to evaluate ER and PR status on the specimens sent to Imam hospital. FMCs were confirmed by the attended pathologist using H&E staining. Resulting data are shown as relative frequency percentages.

3. Results

The results of this study are presented as what follows:

Breed: Out of 40 cases; our study consisted of mostly DSH breed (52.5%).

a. Domestic short hair – 21 (52.5%)
b. Domestic long hair – 13 (32.5%)
c. Persian – 6 (15%)

Sex: All obtained cases were females.

Age: Four age groups were considered based on reported cases, mostly 9-12 years old queens (52.5%) (Chart 1).

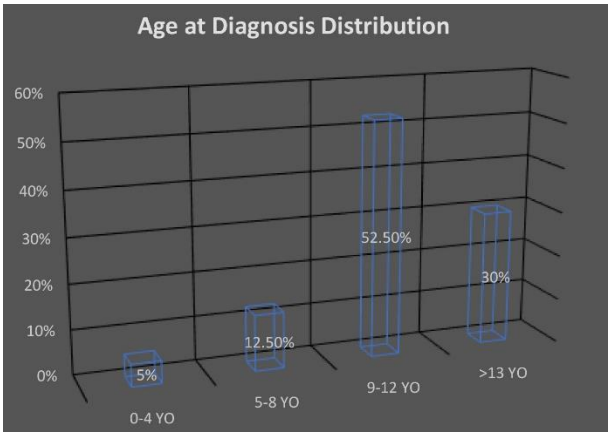

Chart 1. Age distribution

Tumor Size

Tumor sizes were divided into 3 groups and were measured in centimeters. Most of the represented tumors (57.5%) fell into more than 3 cm group (Table 1).

Table 1. Tumor size

Tumor Size	No. of cases
<2 cm	5 (12.5%)
2-3 cm	12 (30%)
>3 cm	23 (57.5%)

Diet Type

Types of food were recorded using a checklist. In cases of mix rations, they were classified in terms of more used type of food. Most of this study cases consumed homemade food (65%) (Table 2).

Table 2. Diet type

Diet type	No. of cases
Homemade	26 (65%)
Commercial	14 (35%)

Reproductive status

Neutered and intact females were recorded on the day of presentation. Study cases were mostly intact (85%) (Table 3).

Table 3. Reproductive status

Reproductive status	No. of cases
Spayed	6 (15%)
Intact	34 (85%)

Parity

Three groups for this criterium were created. Queens mostly had no litter (57.5%) (Table 4).

Table 4. Parity

No. of litters	No. of cases
None	23 (57.5%)
1	7 (17.5%)
2	8 (20%)
>2	2 (5%)

Body Condition Score (BCS)

We used a three-point scale to determine BCS. BCS score 3 consisted most of the study cases (67.5%) (Table 5).

Table 5. Body condition score

BCS	No. of cases
1	5 (12.5%)
2	8 (20%)
3	27 (67.5%)

Multiple Tumors

Occurrence of multiple tumors were recorded through physical examination. Most cases had multiple tumors (67.5%) (Table 6).

Table 6. Number of tumors

Multiple Tumors	No. of cases
Yes	27 (67.5%)
No	13 (32.5%)

Estrogen Receptor (ER) and Progesterone Receptor (PR) Status

Immunohistochemistry was used to determine ER and PR status. Most of the represented cases were ER (55%) and PR (57.5%) positive (Table 7).

Table 7. ER and PR status

ER	No. of cases
Yes	22 (55%)
No	18 (45%)
PR	No. of Cases
Yes	23 (57.5%)
No	17 (42.5%)

Location of Tumors

Cats usually have 4 pairs of mammary glands, with 5th inguinal pair being so rare. The location of tumors was examined and recorded on the day of presentation. FMCs were mostly occurred on abdominal mammary glands (65%) (Chart 2).

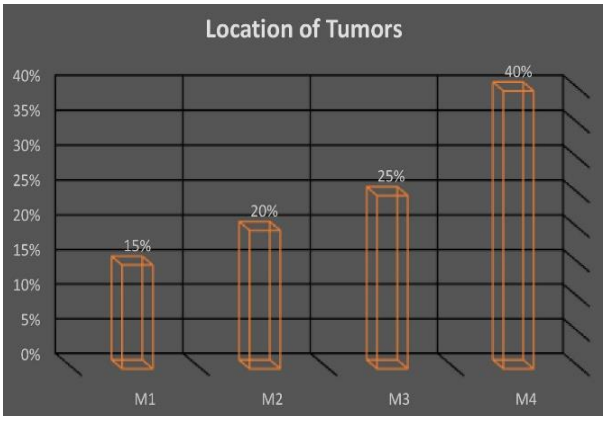

Chart 2. Location of tumors (M1= right and left cranial thoracic mammary glands; M2= right and left caudal thoracic mammary glands; M3= right and left cranial abdominal mammary glands; M4= right and left caudal abdominal mammary glands)

Type of Treatment

Three treatment types were applied. More than two thirds of the cases were treated with mastectomy alone (77.5%) (Table 8)

Table 8. Treatment types

Treatment	No. of cases
Mastectomy	31 (77.5%)
Mastectomy + Chemo	6 (15%)
None	3 (7.5%)

Histopathological Findings

Histopathological findings were observed and recorded by certified attended pathologists at the determined hospitals (Figure 1).

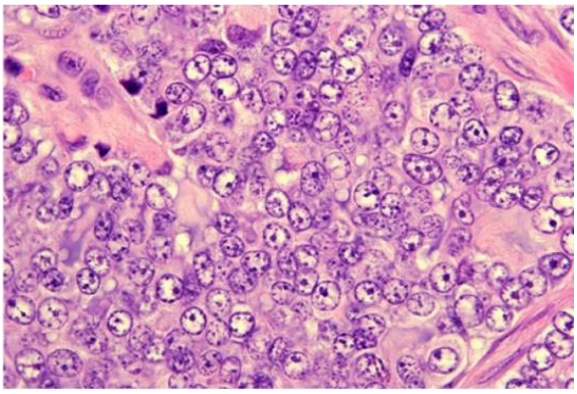

Figure 1. Mammary gland carcinoma, H&E staining (200X magnification)

4. Discussion

In this study, domestic short hairs had higher occurrence of FMCs compared to other breeds, which was consistent with the work of Hayes et al. and Withrow et al [15, 16]. The reason behind this predisposing factor is still unclear but the far larger population of domestic short hairs compared to other breeds may play a role in more frequent report of FMC.

Age was directly associated with FMC occurrence and malignancy [17]. Queens in the age range of 9-12 years had the most FMCs followed by more than 13 years old queens. Our results confirm previous studies [17-20]. As proposed by previous studies, risk increases with age but does not make significant change until 9 years of age [10]. In humans, also, breast cancer incidence elevates with age [21].

FMC was more prevalent in intact females (85%); this finding is in complete agreement with those of prior research [14, 15, 17]. There is a strong relationship between females being intact and FMC occurrence. It is reported that intact females have a seven-fold higher risk than spayed queens [10, 22]. Also, the age of performing OHE is vital. Queens neutered before six months had the best results, while there was no significant benefit in neutering after 24 months [14]. This can be explained by the role of sex hormones in developing FMC. The effect of sex hormones on the pathology of mammary carcinomas is well-documented. In Europe, regular administration of progestogens to prevent estrus in female cats elevated the risk of FMC [23]. Also, in another report, out of 22 cases of male mammary carcinomas, 8 (36%) had a history of progestogen use [24].

Parity is another studied risk factor. In human medicine literature, it is established that having multiple children or giving birth at a younger age decreases breast cancer [25, 26]. In our study, most of the reported queens with FMC had no litter (57.5%). The influence of having multiple litters or having litters, in general, is not especially studied in cats, but in the study of Wood et al., most cats (84.2%) were nulliparous [27]; however, they did not claim that this factor directly impacted their results. In the study of Overley et al., most of the cats diagnosed with mammary carcinoma did not have litters [14], yet when the cats were stratified in terms of age, that significant difference disappeared. Conclusively, there is no general agreement on the effect of parity on FMC and thus more research is needed.

Tumor size is occasionally used as a marker for staging cancer. Most of the tumor sizes in this study was lesser than 2 cm (57.5%), which is in good agreement with previous studies [10, 28]. Tumor size is also correlated with proliferation activity of tumor cells and some scholars used this as a criterium for survivability [29].

There was a direct relationship between FMC occurrence and a homemade diet, 65% of FMC-positive cases were fed using homemade food, which may be due to the precise formulation of commercial foods and tailoring them for cats. However, the effect of diet type on FMC has not been studied properly, but homemade food was a risk factor for dogs in the study of Zatloukal et al [30] and Varma et al. [1]. Obesity is another studied risk factor that could result from excessive diet energy. Scholars use body condition scoring to determine obesity. In our study, 67.5% of cases were obese (grade 3 on our 3-point scale). In women, there is a direct relationship between obesity and breast cancer [31]. In dogs, also, obesity is related to mammary cancer [6]. Although overweight cats have more leptin levels in their serum, cats with mammary carcinoma showed decreased free leptin index [31]. Thus, more studies are needed to elaborate on the role of obesity/leptin in FMCs.

A little more than half of our cases were ER (55%) and PR (57.5%) positive. Although many researchers reported most of FMCs to be ER and PR negative, more than one third put an emphasis on the role of PR in tumor development [10, 28, 32, 33]. These discrepancies may result from the variance in case selection or methods.

Most of the mammary tumors were present in abdominal glands (65%); this finding is in complete agreement with those of previous studies [34]. Also, that most of the cases had multiple tumors (67.5%) is consistent with what was reported in previous studies

[19].Surgery is almost invariably exists in all protocols of treatment and sometimes performs alongside chemotherapy in cases of delayed diagnosis [10]. In our study, most of the cases (77.5%) were treated by surgery alone, which is a good sign of early detection.

5. Conclusion

Domestic shorthair has more tendency to develop FMC. Middle-aged to old-aged intact queens were more in danger of FMC. Having no litter, homemade diet, obesity, PR and ER positive status are considered as other important determinants in FMC occurrence. Homemade diet may contribute to FMC due to its unbalanced formulation. Due to many epidemiological and physiological similarities between cats and humans, FMC can be used as a model to study human breast cancer.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the University of (Code: IR.UT.VETMED.REC.1401.003)

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Author's contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declare no conflicts of interest.

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