Proceedings of the 36th World Small Animal Veterinary Congress
WSAVA

Oct. 14 - 17, 2011
Jeju, Korea

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MAMMARY GLAND TUMORS IN CATS:
RISK FACTORS, CLINICAL PRESENTATION,
TREATMENTS AND OUTCOME

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Abstract
Mammary tumors affect older female cats. The majority of tumors are malignant and associated with aggressive behavior. Early detection and radical surgery is associated with more favorable outcome. Cats with large tumors and/or aggressive histology have a poor prognosis despite systemic chemotherapy.

Epidemiology and etiology
Mammary tumors represent the 3rd most common neoplasia in cats and are not as common in cats as in dogs¹. However, despite the overall lower incidence when compared to dogs, mammary tumors nevertheless represent a significant health problem in cats because of the higher rate of malignancy and the more aggressive clinical behavior. The main risk factors developing mammary tumors in cats include hormonal influence, age and breed¹.

Hormonal influence: Hormonal influences play a major role in mammary tumor development also in cats. Sexually intact cats have a 7-fold increased risk for mammary tumors compared to spayed cats¹. However, OHE must be performed early in life in order to be protective: The protective effects diminish quickly over the first few years as illustrated by a risk reduction of 91%, 86% and 11% depending on whether the cat is spayed before 6 months, between 7-12 months, or 13-24 months, respectively². There appears to be little to no benefit after the first 24 months. Exposure to exogenous progestins also increases the tumor risk in the cat. Cats treated with progestins were found to have an overall relative risk of 3.4 compared to cats that did not receive such treatments. Benign tumors are more common than malignant tumors in progestin-treated cats³. The tumorigenic effects of progestins in cats are also illustrated by the reports of mammary tumors in male cats. In general, mammary tumors are rare in males, but according to a large case series on mammary cancer in male cats 8/22 cats had a history of progestin use⁴.
Age: Mammary neoplasia is a disease seen predominantly in middle aged to older cats. The mean age of tumor diagnosis is between 10-12 years. Malignant tumors are rare in younger cats, but fibroepithelial hyperplasia, a progestin-induced diffuse mammary gland enlargement of the can be seen in very young intact cats.

Breed: Several studies have reported that Siamese cats are over-represented when compared to other cat breeds. Interestingly, Siamese cats also develop mammary tumors at an earlier age than other breeds supporting a genetic predisposition for mammary tumors.

Clinical presentation
Mammary tumors are relatively easy to detect on physical exam. The tumors appear as relatively firm discrete mass(es) in the mammary gland(s). Multiple tumors are common; one study reported that 60% of the cats had more than one tumor at diagnosis. The size of the tumor(s) at diagnosis, presence or absence of ulceration, fixation and enlarged lymph nodes depend on when in the course of disease the tumors are detected and diagnosed. Inflammatory mammary carcinomas in cats are rare, but can occur also in cats. Most cats that receive regular veterinary care are likely to be diagnosed prior to signs of systemic illness. Nevertheless, due to the high rate of malignancy and the fact that most of these cats are older, and may have unrelated medical problems, a complete blood count, serum chemistry panel, complete staging, including tumor measurements, lymph node assessment and 3 view thoracic radiographs should be performed prior to surgery.

Staging system: A modified WHO staging system is used to stage feline mammary tumors. The system is based on the T (tumor size) N (lymph node status) and M (metastasis) system. see Table 1.

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Tumor size</th>
<th>Lymph node status</th>
<th>Metastasis</th>
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<tbody>
<tr>
<td>T1 &lt; 2 cm</td>
<td>NO</td>
<td>MO</td>
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| Stage 2 | T2 2-3 cm | NO | MO |

| Stage 3 | T1,2 < 3 cm | N1(positive) | MO |
| T3 > 3 cm | NO or N1 | MO |

| Stage 4 | Any | Any | M1(metastasis) |

Note that stage 3 disease includes cats with small tumors (T1 and T2; < 3 cm) and positive lymph nodes (N1) as well as cats with larger tumors (> 3 cm) regardless of lymph node status.

Prognostic factors
Tumor size is one of the most consistent prognostic factors in feline mammary carcinoma. Cats with tumors less than 2 cm or 8 cm3 can have an excellent long term survival (> 3 years) if treated with surgery alone (radical mastectomy) according to a prospective and retrospective studies in cats. These prolonged survival times have not been reproduced by later studies despite the fact that cats in these studies also received adjuvant chemotherapy. There is however a general agreement that cats with tumors larger than 3 cm (27 cm3) have a poor prognosis.
Lymph nodes: Cats with positive regional lymph nodes have a poor prognosis. According to a recent study all cats with positive local lymph nodes were dead within the first 9 months. These findings are biologically plausible; metastasis to the lymph node confirms metastatic ability and implies systemic involvement, and therefore an indication for systemic therapy.

Age and breed: Several retrospective studies have reported a worse prognosis in older cats. However, these results may be biased due to potential differences in stage and treatment choices in older cats. According to a large prospective randomized trial, there was no difference in outcome according to age. Thus, age itself should not be a factor when considering treatment for cats with mammary carcinoma as long as the cat is otherwise healthy. According to the same study, domestic shorthair cats did significantly better than purebred cats.

Histopathological prognostic factors: 80-90% of mammary tumors in cats are malignant. Adenocarcinoma is the most common type. Histological grade using a similar scoring system as described in dogs (grade I, grade II and grade III) can be used to identify cats with more aggressive tumors. Two independent studies confirmed that cats with grade III tumors had a significantly shorter survival than cats with lower grade tumors. Additionally the presence of vascular invasion regardless of tumor size and grade was associated with a worse prognosis according to one of these studies.

Treatments and outcome

Surgery is the mainstay of treatment for cats with mammary tumors. Radical mastectomy of the entire ipsilateral chain has become the standard surgical procedure in cats. Bilateral radical mastectomy should be performed in cats with tumors in both chains. This standard is based on results from a retrospective study comparing remission and survival in cats treated with conservative surgery versus radical surgery. Cats treated with radical surgery (whole chain plus inguinal lymph nodes) had a significantly longer remission than cats treated with a more conservative procedure (removal of affected gland and adjacent gland). The difference in remission suggest that prophylactic mastectomy of normal glands is beneficial by preventing new tumors in the affected chain, thus a longer remission. However, the type of surgery does not affect survival, reflecting that this is a highly aggressive cancer and cause of death in most of these cats is metastatic disease. Results from a later study suggested that bilateral mastectomy may be superior to unilateral mastectomy, however, this was also a retrospective study and information regarding tumor size and grade in the subgroup treated with bilateral mastectomy was not provided. Bilateral radical mastectomies are aggressive procedures resulting in longer recovery time, and may need to be staged in some cats.

Chemotherapy: Despite the poor outcome and the high incidence of metastatic disease in cats diagnosed with large tumors and unfavorable histopathology, few advances have been made regarding systemic therapy in cats with mammary carcinomas. Several retrospective reports describe outcome in cats treated with adjuvant doxorubicin based chemotherapy. Interestingly, none of these reports reproduce the prolonged survival reported in cats with stage I disease treated with surgery alone. Early diagnosis and aggressive surgery is associated with a better prognosis in cats with mammary carcinoma. However, further research and prospective trials to indentify effective drugs to prevent or delay metastasis is desperately needed.
References


