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Complex carcinomas of the mammary gland in cats: Pathological and immunohistochemical features

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Abstract

Biphasic epithelial myoepithelial (complex) carcinomas of the feline mammary gland are rare. This article describes the pathological and immunohistochemical features and clinical outcome of eight cases of feline mammary carcinomas displaying complex morphology. This tumour type is a low grade malignancy that shows histopathological features distinctive from more common feline mammary carcinomas and from complex mammary carcinomas of dogs. It appears to have a better overall survival than other carcinomas of the mammary gland of cats.

Keywords: Complex carcinoma; Epithelial-myoepithelial carcinoma; Feline tumours; Immunohistochemistry; Mammary gland

1. Introduction

Biphasic epithelial myoepithelial (complex) carcinomas of the mammary gland, characterized by the presence of two cell populations, epithelial luminal cells and myoepithelial cells, are commonly observed in canines, and are associated with better prognosis than simple carcinoma (Misdorp et al., 1999; Rutteman et al., 2001). Complex carcinomas of the feline mammary gland are rare, and the effect of the presence of myoepithelial cells on prognosis is unknown. Moreover, there are not sufficient studies to permit the classification of feline carcinomas according to their prognostic histological features (Misdorp et al., 1999).

We describe here the morphological features, and clinical behaviour of eight cases in cats of epithelial-myoepithelial mammary tumours, a tumour type apparently associated with a better prognosis than other common feline mammary carcinomas (FMCs).

2. Materials and methods

Eight cases of complex carcinomas from female cats were identified among the surgical pathology material of the Histopathology Laboratory of the University of Trás-os-Montes e Alto Douro (UTAD) over a 2-year period. All samples were surgically obtained by simple mastectomy. Formalin fixed and paraffin-embedded sections were stained with haematoxylin and eosin (H&E). Neoplasms were classified according the most prominent growth pattern. To confirm the biphasic pattern of the tumour additional sections were immunostained with a panel of antibodies using streptavidin-biotin-peroxidase method. The markers used were: Vimentin (1:100, NCL-Vim-Va, Dako), Cytokeratin (CK) AE1/AE3 (1:50; Dako), Cytokeratin 14 (1:20; NCL-LL 002, Novocastra), p63 (1:150, 4A4, Neomarkers), and Calponin (1:400, CALP, Dako).

Immunohistochemical data were evaluated as positive (+), negative (−) or inconstant positivity (+/−) for p63 (nuclear), CK AE1/AE3 and calponin (cytoplasmic positivity). The immunoreactivity of CK14 and vimentin staining was assessed semi-quantitatively in the luminal compartment as negative (−); (+) when fewer than 5% of the cells were positive; (++) when 5–25% of the cells were positive; (+++) when 25–50% of the cells were positive and (++++) when more than 50% were positive cells. Stromal and non-neoplastic mammary gland tissue adjacent to the tumour was used as controls.

An analysis of outcome was performed to determine the prognostic value of this biphasic phenotype using univariate methods. The queens included in this study were followed for at least 24 months after surgery by

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the referring veterinary surgeons to evaluate the post-surgical course of the disease. Survival rates were compared with 45 other common invasive mammary carcinomas of non-specified type, observed in the same period of time in UTAD's Laboratory. The simple type phenotype of these tumours was confirmed using the basal/myoepithelial markers described previously. This tumour group showed pathological characteristics classically reported for feline mammary carcinoma: large lesions (29/45 >2 cm), high grade (24/45 grade 2 and 19/45 grade 3), high stage (19/45 stage 3), frequent emboli (33/45) and regional lymph node metastases on presentation (14/45). Overall survival was defined as the time from the date of surgery until the date of death or the last follow-up.

Disease free-survival was defined as the period of time between surgery and recurrent or metastatic disease. Survival rate was calculated by the Kaplan–Meier method, and statistical significance was examined using a log-rank or Breslow test. $P < 0.05$ was considered statistically significant.

3. Results

The clinical and epidemiologic data of the female cats are shown in Table 1. Macroscopically complex carcinomas were well delineated, firm, greyish-white solid masses measuring 0.8–4 cm at the greatest diameter (mean 1.7 cm). The mean age of the animals was 7.7 years (range 4–14 years), and breeds included four Siamese, three European Domestic Shorthair and one cross-bred with a Persian cat. Four (50%) queens had received hormonal treatment with synthetic progestins for an unknown period of time.

Histological analysis revealed expansile, well-delimited but non-encapsulated neoplasms, forming small nests and sheets admixed with ductular structures, separated by thin fibrous stroma. The trabecular (solid) pattern was the most prominent growth pattern observed (62.5%; $n = 5$), although tubular areas were present in seven (87.5%) carcinomas on study (Fig. 1). Some nodules showed slit-like spaces like fibroadenomas and focal papillary areas. The less frequent growth pattern observed was the intraductal papillary-cystic. With the exception of one multinodular case with papillary-cystic architecture, all lesions were single nodules.

Two cell types were identified: the central or luminal cells surrounded by a continuous peripheral layer of neoplastic myoepithelial cells. The epithelial cells were small cuboidal to oval with round hypercromatic nuclei and scant cytoplasm. The myoepithelial cells were round, spindle-shaped or polyhedral, variable in size with irregularly shaped euchromatic nuclei, and clear or eosinophilic cytoplasm with indistinct cytoplasmatic borders (Fig. 2). Sometimes we observed solid masses of spindle-shaped or polyhedral cells.

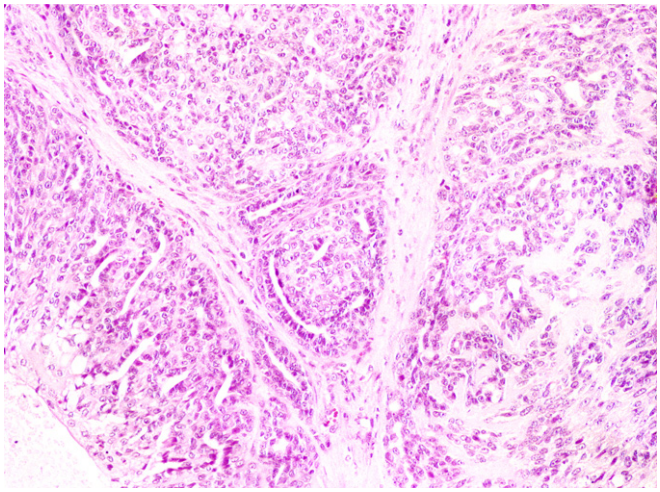

Fig. 1. Complex carcinoma showing tubular structures and trabeculae. H&E, 20×.

Cytological atypia was mild (62.5%; $n = 5$) to high (37.5%; $n = 3$) and not restricted to the epithelial component. Atypical epithelial and myoepithelial cells had large, pleomorphic, vesicular nuclei containing prominent nucleoli. Mitotic figures and necrosis were uncommon and all tumours but one presented rounded, pushing margins with small foci of stromal invasion. No vascular invasion was seen. One cat (case 8) had a poorly differentiated complex carcinoma with high nuclear grade and high mitotic activity in both epithelial and myoepithelial cell populations. Lymph node metastases were observed in this tumour, in which only the epithelial component was present.

Some tumours presented foci of squamous metaplasia (cases 2 and 8) and osteoclastic-like multinucleated giant cells (cases 1, 5 and 6). In all but one case, inflammatory

Table 1
Clinical and pathological data

Case number	Breed	Age (years)	Contraception	Nodule size (cm)	Predominant growth pattern	Follow up
1	Siamese	10	NA	1.5	Trabecular	NT after 31 months; AW after 39 months;
2	Siamese	10	Yes	0.8	Papillary	AW after 34 months
3	Siamese	4	NA	1.0	Tubular	NT after 14 months; AW after 22 months
4	European	6	NA	0.8	Papillary-cystic	Lost to follow-up
5	European	8	Yes	2.2	Trabecular	AW after 28 months
6	European	6	Yes	4.0	Trabecular	Did not recover from surgery
7	Siamese	4	NA	1.0	Trabecular	Lost to follow-up after 5 months
8	Cross breed	14	Yes	2.4	Trabecular	Euthanased after 7 months

(NA, Data not available; AW, Alive and Well; NT, new tumours).