



Study on histopathological subtypes and grading of canine mammary tumours

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Abstract

The incidence of mammary neoplasms is more in dogs when compared to other animals. Mammary neoplasms are among the most prevalent type of tumours in bitches, followed by skin tumours. Canine mammary tumour (CMT) and human breast cancer (HBC) have clinical and molecular similarities, making CMT a good model to study HBC. A study was conducted on 25 cases of CMT in bitches which were presented during a period from March 2019 to March 2020 to University Veterinary Hospitals at Mannuthy and Kakkalai. Tumours were histologically classified basically into carcinoma, sarcoma, carcinosarcoma, benign tumour and further its subtypes were identified. Out of total 25 CMTs, only one case was identified as benign, while all the other cases were found to be malignant. Modified Elston and Ellis grading method was used for histological malignancy grading of CMT. Histological malignancy grading done in 23 cases revealed grade I (30.43 per cent), grade II (60.87 per cent) and grade III (8.7 per cent) malignancy. Sixty-five per cent of simple carcinomas, which included ductal carcinoma, tubulo-papillary carcinoma, solid carcinoma, comedocarcinoma and cribriform carcinoma, were either grade II or III, while all the mixed tumours were grade II. The present study revealed that histological malignancy grading could be used as a tool for predicting prognosis of CMT.

Keywords: Canine mammary tumour, histological classification, grading

Dogs can be used as a model to study human breast cancer due to the genotypic and phenotypic similarities of this tumour in both species. Through whole exome and transcriptome analysis, researchers discovered similarities in genomic characteristics in 191 spontaneous canine mammary tumours (CMT) that exhibited the archetypal features of HBCs, including frequent

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PIK3CA mutations (43.1%), PI3K-Akt pathway aberrations (61.7%), and key genes involved in cancer initiation and progression (Kim *et al.*, 2020). Highest occurrence of CMT cases were reported in 8-12 year aged dogs, followed by 4-8 years, while least occurrence was reported in dogs less than 4 years of age (Dhami *et al.*, 2010). Canine mammary tumour may affect either multiple or single gland, and majority of the cases were noticed in inguinal mammary gland followed by caudal abdominal gland (Kumar and Parasar, 2020). Breed predisposition in the occurrence of CMT is not established yet, which may be due to the fact that it may vary in accordance with breed preferences in different populations under study. Histological evaluation is considered as the cornerstone for classifying CMTs. Goldschmidt *et al.* (2011) published a histological classification scheme for CMTs, which emphasized architectural arrangements of neoplastic cells and involvement of myoepithelial cells in the neoplastic process. Analysis of the histopathological subtypes helps in understanding the prognosis of the disease. Histological malignancy grading is also used as a tool for predicting prognosis of CMT. Three histological features used in grading of CMTs are the extent of tubule formation, nuclear pleomorphism and mitotic figures. Tubule formation reveals degree of structural differentiation in the tumour. Nuclear irregularity is associated with worse prognosis. As the tumour invasion is taking place in the periphery of tumour, mitotic activity and nuclear pleomorphism are assessed better in the peripheral area. These three features provide a good correlation with prognosis of the tumour and have the advantage of simplicity in the method (Bloom and Richardson, 1957).

Materials and methods

Twenty-five cases of spontaneous mammary tumours in pure or mixed breed bitches in the age group of 3 to 15 years, presented during March, 2019 to March, 2020, at University Veterinary Hospitals of Mannuthy and Kokkalai were utilised for the study. After surgical treatment, the excisional biopsy samples were collected and immediately fixed in 10% neutral buffered formalin. After 48 hours of fixation, these samples were processed by routine paraffin embedding method and sections were stained with haematoxylin and eosin (Suvama *et al.*, 2019).

Histopathological evaluation

Stained sections of tumour samples were examined under light microscope and classified histologically according to the method described by Goldschmidt *et al.* (2011). Mammary gland affections were classified into malignant epithelial neoplasms, malignant epithelial neoplasms- special types, sarcomas, carcinosarcomas, benign neoplasms, hyperplasia/dysplasia, neoplasm/hyperplasia/dysplasia of nipple.

Grading of canine mammary tumours

Histological malignancy grading (HMG) was done based on the modified Elston and Ellis grading method employed in human breast cancer (Clemente *et al.*, 2010). The grade was assessed by considering three features which included tubule formation, nuclear pleomorphism and mitotic counts, each feature being scored 1 to 3 points.

Table 1. Histopathological subtypes and their respective histological malignancy grading

Tumour type	Grade I	Grade II	Grade III	Total
Ductal carcinoma	6	7	1	14
Tubulo-papillary carcinoma	0	3	0	3
Solid carcinoma	0	1	0	1
Comedocarcinoma	0	0	1	1
Cribriform carcinoma	1	0	0	1
Carcinosarcoma	0	3	0	3
Total	7	14	2	23

Tubule formation in the stained section was assessed and a score of one point was given when more than 75 per cent of the area was composed of definite tubules. Two and three points were given respectively when 10-75 per cent and < 10 per cent of the area was covered by tubules.

A score of one was assigned when the nuclei were small with minimum variation in size and had uniform chromatin, while a score of two was given when the nuclei were larger in size with moderate anisokaryosis. When nuclei were vesicular, varying considerably in size and shape and bearing prominent nucleoli, a score of three was given.

Mitotic activity was assessed at a magnification of 400X (high power field, HPF), which provided a field area of 0.237 sq.mm. A minimum of 10 fields were examined. Up to nine mitoses per 10 HPF were given one point, 10-19 mitotic figures per 10 HPF scored two points and 20 or more mitotic figures per 10 HPF were given three points. After scoring in each of the above aspects, the scores were added to get a number between three and nine. Then the grade was allocated as below:-

HMG I (low grade) - three to five points, well differentiated

HMG II (intermediate grade) - six or seven points, moderately differentiated

HMG III (high grade) - eight or nine points, poorly differentiated

Results and discussion

In the present study, out of total 25 CMTs only one case was identified as benign, while all the others were found to be malignant. Malignant cases included ductal carcinoma (Fig. 1), tubulo-papillary carcinoma, carcinosarcoma (Fig. 2), solid carcinoma (Fig. 3), comedocarcinoma, mesenchymal spindle cell sarcoma and cribriform carcinoma. Many layers of proliferating glandular epithelial cells enclosing a slit-like lumen were noticed in ductal carcinomas. Solid carcinoma was made up of solid sheets of cells with no lumen in the centre. The presence of aggregates of neoplastic epithelial cells with a central region

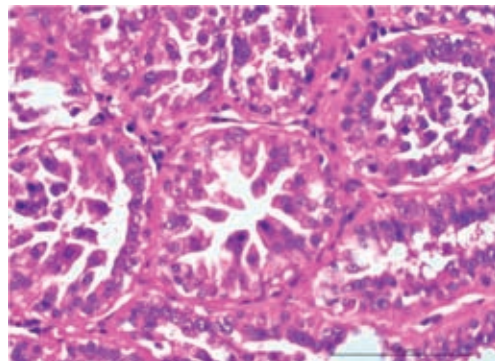


Fig. 1. Ductal carcinoma - proliferating neoplastic cells within duct lumen (H&Ex400)

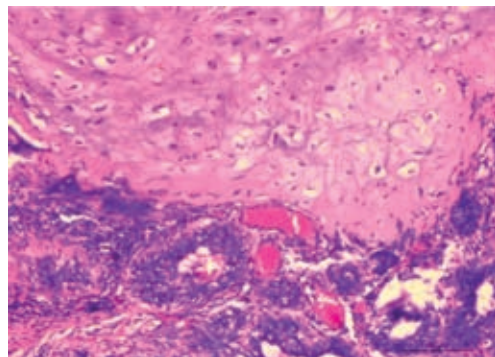


Fig. 2. Carcinosarcoma - both epithelial and mesenchymal portions exhibit neoplastic changes (H&Ex200)

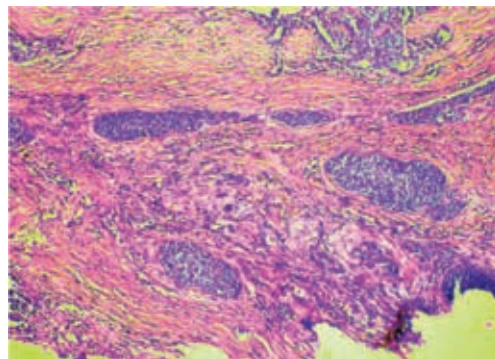


Fig. 3. Solid carcinoma - neoplastic cells proliferate as solid sheets inside duct without any lumen (H&Ex100)

of necrosis was found to be a characteristic feature in comedocarcinomas. Tubulo-papillary carcinoma was pedunculated and made up of proliferating papillary epithelial cells. Cribriform carcinoma was made up of clusters of neoplastic epithelial cells arranged in a sieve-like pattern. Carcinosarcoma was characterised by cells that resembled epithelial and connective tissue components, all of which were malignant.

Histological malignancy grading is used as a tool for predicting prognosis of CMT. In this study, histological malignancy grading done in 23 cases adopting a modified version of Elston and Ellis numeric system (Elston and Ellis, 1993), revealed grade I (30.43 per cent), grade II (60.87 per cent) and grade III (8.7 per cent) CMTs. Histopathological subtypes and their respective histological malignancy grading are shown in table 1. Sixty-five percent (13/20) of simple carcinomas, which included ductal carcinoma, tubulo-papillary carcinoma, solid carcinoma, comedocarcinoma and cribriform carcinoma, were graded as II or III. Studies conducted done by Rezaie *et al.* (2009), also revealed that most of the grade II and III CMTs were simple tumours. However, all the mixed tumours in the present study were of grade II, which was in accordance with Mathew *et al.* (2019). So, it is evident from the study that histological grading is an effective tool in assessing malignancy and predicting prognosis of CMTs.

Conclusion

A gross and histopathological study was conducted on 25 canine mammary tumour cases. Histological malignancy grading was done for each case and the result was correlated with the subtype of CMT. It is evident from the present study that the histological malignancy grading can be used as a very effective tool for predicting prognosis of CMT.

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Conflict of interest

The authors declare that they have no conflict of interest.

References

Bloom, H.J.G. and Richardson, W.W. 1957. Histological grading and prognosis in breast cancer: a study of 1409 cases of which 359 have been followed for 15 years. *Br. J. Cancer*. **11**(3): 359-377.

Clemente, M., Perez-Alenza, M.D., Illera, J.C. and Pena, L. 2010. Histological, immunohistological, and ultrastructural description of vasculogenic mimicry in canine mammary cancer. *Vet. Path.* **47**: 265-274.

Dhami, M.A., Tank, P.H., Karle, A.S., Vedpathak, H.S. and Bhatia, A.S. 2010. Epidemiology of canine mammary gland tumours in Gujarat. *Vet. Wld.* **3**(6): 282-285.

Elston, C. W. and Ellis, I. O. 1993. Method for grading breast cancer. *J. Clin. Pathol.* **46**(2): 189.

Goldschmidt, M., Pena, L., Rasotto, R. and Zappulli, V. 2011. Classification and grading of canine mammary tumours. *Vet. Path.* **48**: 117-131.

Kim, T.M., Yang, I.S., Seung, B.J., Lee, S., Kim, D., Ha, Y.J., Seo, M.K., Kim, K.K., Kim, H.S., Cheong, J.H. and Sur, J.H. 2020. Cross-species oncogenic signatures of breast cancer in canine mammary tumours. *Nat. Commun.* **11**(1): 1-13.

Kumar, P. and Parasar, M.C. 2020. Occurrence of mammary tumour in dogs. *J. Agric. Res. Adv.* **2**: 29-32.

Mathew, R., Sajitha, I. S., Nair, S. S., Krishna, B. D. and Abraham, M. J. 2019. Canine mammary tumours: Histological malignancy grading as a prognostic indicator. *Pharma. Innovation.* **8**(4): 149-151.

Rezaie, A., Tavasoli, A., Bahonar, A. and Mehrazma, M. 2009. Grading in canine mammary gland carcinoma. *J. Biol. Sci.* **9**: 333-338.

Suvarna, S.K., Layton, C., Bancroft, J.D. and Gamble, M. 2019. *Theory and Practice of Histological Techniques* (8th Ed.), Elsevier Health Sciences, 573p.