STEREOLOGICAL ESTIMATION OF MEAN NUCLEAR VOLUME AS A PROGNOSTIC FACTOR IN CANINE MAST CELL TUMOURS

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Introduction: Cutaneous mast cell tumour (MCT) Patnaik and Kiupel grading schemes rely on qualitative and semiquantitative features susceptible to interobserver variability. Stereological estimation of volume-weighted mean nuclear volume (MNV) provides information about both size and variability of nuclear size, which has been proven to have a prognostic value in other solid tumours. The objective was to compare MNV with MCT grade and biological behaviour.

Materials and Methods: Fifty-six MCTs were graded according to Patnaik and Kiupel by consensus of three experienced pathologists. Clinical history of dogs treated with surgical excision alone was collected with a minimum follow-up period of 1 year ($n = 31$). MNV was estimated using the point-intercept method on vertical sections in 10 microscopical fields, with an approximately constant distance proportional to overall sectional area. Animals were divided according to outcome: group 1, no recurrence; group 2, local recurrence, lymph node or distant metastasis. Statistical analyses of results were performed by the Mann–Whitney U Test and receiver operating characteristics (ROC) curve.

Results: MNV of low grade ($n = 35$) and high grade ($n = 20$) was 139.6 ($\pm$ 35.2) μm^3 and 222.9 ($\pm$ 80.4) μm^3, respectively. MNV of grade II ($n = 39$) and grade III ($n = 16$) was 145.6 ($\pm$ 38.6) μm^3 and 229.0 ($\pm$ 88.6) μm^3, respectively ($P < 0.0001$, Mann–Whitney U test). An optimal cut-off value of MNV $> 169\ \mu m^3$ (81% sensitivity and 78% specificity) was shown to differentiate MCTs with a more aggressive behaviour (group 2).

Conclusions: The present study suggests that estimation of MNV on routine histological sections may objectively improve the detection of more aggressive MCTs.

PERITUMOURAL MUM1$^+$ PLASMA CELLS ARE ASSOCIATED WITH POOR OUTCOMES IN CATS WITH INVASIVE MAMMARY CARCINOMA, SPONTANEOUS IMMUNOCOMPETENT ANIMAL MODELS OF BREAST CANCER

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Introduction: Feline invasive mammary carcinomas (FMCs) are considered valuable immunocompetent animal models of breast cancer. Tumour-associated plasma cells have been associated with poor prognosis in breast cancer, but have not been characterized in FMCs. The aim of this study was to determine the amount and prognostic value of peritumoural MUM1$^+$ plasma cells in FMCs.

Materials and Methods: Retrospective study of 180 female cats treated by surgery alone for an invasive mammary carcinoma, with 2-year follow-up. MUM1 (clone MRQ43), FoxP3 (clone SP97), oestrogen receptor (OR) (clone C311), progesterone receptor (PR) (clone 10A9), Ki67 (clone MIB1) and HER2 (clone 4B5) expressions were determined by automated immunohistochemistry. MUM1$^+$ plasma cells and FoxP3$^+$ regulatory T cells (Tregs) were quantitated in intratumoural and peritumoural locations.

Results: Peritumoural plasma cell enrichment was positively associated with larger tumour size ($\geq$10 mm; $P = 0.03$), dermal infiltration ($P = 0.006$), and increasing numbers of intratumoural Tregs ($P = 0.001$). By multivariate survival analysis, luminal (OR$^+$ and/or PR$^+$) FMCs (57/180; 32%) with high numbers ($>287/mm^2$) of peritumoural plasma cells (43/57; 75%) were associated with shorter overall survival (hazard ratio [HR] = 2.56, 95% confidence interval 1.23–5.26) independently of PR expression (HR = 0.40 for PR$^+$ FMCs), and low nuclear polymorphism (HR = 0.41; $P = 0.0001$; Cox proportional hazards regression). The negative impact of peritumoural plasma cells on overall survival was also observed in triple-negative (OR$^-$, PR$^-$, HER2$^-$) FMCs (123/180; 68%).

Conclusions: FMCs enriched in peritumoural plasma cells are enriched in Tregs, and associated with a worse outcome. They seem promising animal models to test new cancer immunotherapy strategies in an immunosuppressed tumour microenvironment.