Immunohistochemical expression of lipoxxygenase-5 (LOX-5) in canine normal urinary bladder, cystitis and transitional cell carcinoma

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OBJECTIVES

Canine transitional cell carcinoma (TCC) mimics human invasive TCC. Human TCC overexpress lipoxxygenase (LOX)-5 and the use of target inhibitors has been proved effective. In this study, we investigated the immunohistochemical (IHC) expression of LOX-5 in normal canine urinary bladder, cystitis and TCC. LOX-5, cyclooxygenase

(COX)-1, COX-2 IHC expression and their relationship among the different groups were investigated.

METHODS

Biopsies of cystitis and TCC were reviewed (2012–2016). Dogs were excluded if had received steroids, non-steroidal antiinflammatory drugs (NSAIDs) and/or chemotherapy prior to tissue collection. Samples of histologically normal bladder were retrieved from the necropsy archive. Representative sections were submitted for anti-LOX5, COX-1 and COX-2 IHC. Distribution and intensity were assessed semi-quantitatively and an IHC score was obtained for each marker. Immunohistochemical results were compared among normal epithelium, cystitis and TCCs. Correlations between variables were analysed with Spearman and Mann Whitney.

RESULTS

Twenty-nine TCCs, 13 cystitis and 10 controls were included. All TCCs were diagnosed as invasive and histologically high-grade. Cystitis were characterised by similar lymphoplasmacytic and occasionally neutrophilic infiltrates. LOX-5 was expressed in 95% of TCCs, 23% of cystitis and 10% of controls. LOX-5 and COX-2 IHC scores were significantly ($P < 0.01$) higher in TCCs vs cystitis and normal bladders.

STATEMENT (CONCLUSIONS)

TCC is the most common canine urinary-tract tumour. Chemotherapy is commonly advised, but responses are poor to modest. Results of this study place the rationale for the investigation of new agents such as tepoxalin, an NSAID with anti COX-2 and LOX-5 effect.

Genome-wide analysis of canine oral malignant melanoma (OMM) metastasis-associated gene expression

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OBJECTIVES

Melanoma of the oral cavity is the most common melanocytic neoplasm in dogs and has a high metastatic potential. The study objective was to identify a canine primary OMM pro-metastatic gene expression signature.

METHODS

Canine Gene 1.1 ST Arrays were employed for comparative genome-wide expression profiling of formalin-fixed paraffin-embedded biopsies of 18 canine primary OMM that metastasised and 10 canine primary OMM that did not metastasise. Results were validated by RT-qPCR.

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RESULTS

Differential expression of the C-X-C Motif Chemokine Ligand 12 (*CXCL12*) between the M and NM OMMs suggests that canine OMM metastasis is mediated by interaction between *CXCL12* and *CXCR4*. Increased expression of Apolipoprotein B mRNA Editing Enzyme Catalytic Subunit 3A (*APOBEC3A*) in the M OMMs may be indicative of *APOBEC3A*-induced double-strand DNA breaks and pro-metastatic *APOBEC3A*-mediated hypermutation. DNA double strand breakage triggers activation of the DNA damage response network and two members of the Falconi anaemia DNA repair pathway show elevated expression in the M OMMs.

RT-qPCR analysis validated the greater than two-fold differences in expression between M and NM OMMs observed for 3 genes (*APOBEC3A*, *CXCL12* and *RPL29*). A Linear Discriminant Analysis classifier featuring the 3 genes was estimated to categorise M OMMs as metastasising with an accuracy of 94% and NM OMMs as non-metastasising with an accuracy of 86%.

STATEMENT (CONCLUSIONS)

Metastasis-associated differences in gene expression may highlight genes that constitute targets for anti-metastasis treatments, and that may be effective as predictive biomarkers of OMM metastasis.

Strontium 90 plesiotherapy in the treatment of eyelid squamous cell carcinoma in cats

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OBJECTIVES

Squamous cell carcinoma (SCC) is the most common tumour in cats' eyelid. Aggressive surgery is the treatment of choice, but in some cases a more conservative approach could be considered. Strontium 90 plesiotherapy (Sr90) is a form of radiotherapy targeting superficial tumours. The aim of this study was to describe response, outcome and tolerance of eyelid SCCs treated with Sr90.

METHODS

The clinical database was searched for cats diagnosed with SCC located on an eyelid and treated with Sr90. The response to the treatment was evaluated every 4–6 weeks initially and then every 3 months. Descriptive statistics were applied on data collected.

RESULTS

Eight cats were treated with Sr90 between 2014 and 2017, six as a primary and two as adjuvant treatment. Four cats received a single dose between 100–120 Gy and four cats five fractions in 10 days to a total dose of 140 Gy. Five of six cats treated with primary Sr90 achieved complete response (CR) and one partial response (PR) for an overall response rate of 100%. The five cats achieving CR were free of disease after a median of 17 months, while the cat with PR did not present evidence of progression at 18 months. One cat treated with adjuvant Sr90 was free of disease at 17 months, while the other one died in clinical remission 9 months post-treatment. Acute and late side effects were minimal.

STATEMENT (CONCLUSIONS)

Sr90 provided good local control in this small cohort of cats and was well tolerated.

Correlation between BRAF variant V595E and histological grade in canine transitional cell carcinoma

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OBJECTIVES

Mochizuki et al. (PLoS ONE 2015a, 10(6):e0129534; PLoS ONE 2015b, 10(12):e0144170) found BRAF mutation (Variant c.1784T > A) in 67–75% canine transitional cell carcinomas (TCCs). Maeda et al. detected BRAF mutation in 54.5% of TCC cases (BMC Cancer 2018). In our recent publication the mutation was found in 22 out of 31 (71%) canine TCC cases (Tierärztl. Prax. 5/2018). The objective of the present study was to investigate the correlation of BRAF variant V595E and histological grading of TCC.