

Investigation of immune cell markers in feline oral squamous cell carcinoma

ABSTRACT

Squamous cell carcinoma is the most common oral cancer in the cat and presents as a locally aggressive lesion for which an effective therapeutic protocol remains elusive. Feline oral squamous cell carcinoma (OSCC) shares many clinical characteristics with human head and neck squamous cell carcinoma (HNSCC). Accordingly, present studies were conducted to determine similarities for immune markers shared by feline OSCC and human HNSCC. Biopsies harvested from a feline patient cohort-1 (n = 12) were analyzed for lymphoid cell infiltrates by immunohistochemistry (IHC). Results revealed unique patterns of T cell infiltration involving both neoplastic epithelium and stroma that were detected in most patient tumor biopsies (92%) examined by IHC staining for CD3. Intratumoral B cell infiltrates were detected within tumor stroma only, based on IHC staining for CD79a and CD20 for all patients within the same cohort-1. Infiltration of tumors by a regulatory CD4 T cell subset (Tregs) defined by expression of the forkhead transcription factor FoxP3, was also detected in biopsies from 57% of patients and involved infiltration of neoplastic epithelium and stroma. Patient biopsies were also examined for expression of immunomodulator cyclooxygenase (COX)-2 and revealed positive but weak staining of neoplastic epithelium in a significant proportion of cases (75%). Interestingly, COX-2 expression was detected in both neoplastic epithelium and stroma. Blood collected from a second cohort of feline OSCC patients (n = 9) revealed an increased frequency of circulating CD4+FoxP3+ T cells when compared to healthy adult controls (n = 7) (P = 0.045), although frequencies of CD4+CD25+FoxP3+ T cells were comparable between patients and healthy pet cat controls. Lastly, biopsies from feline OSCC patients were characterized for histologic subtype using a classification scheme previously described for human HNSCC. This analysis revealed the conventional subtype as the predominant variant (75%) with conventional subtypes split evenly between well differentiated and moderately differentiated carcinomas. Two cases were classified as papillary and one case as basaloid subtypes. Correlations between subtype, immune marker scores or circulating Treg frequencies and clinical characteristics or outcome were not detected, most likely due to small patient numbers within patient cohorts. However, findings from these studies provide a preliminary step in the characterization of immune and histologic markers that will be critical to defining prognostic immune markers for feline OSCC and potential targets for testing of immunotherapeutics also relevant to human HNSCC in future studies.

Keyword: Feline oral cancer; Squamous cell carcinoma; Lymphoid cell infiltrates; Tregs; COX-2; Histologic subtypes.