Combination of radiation therapy and a selective COX-2 inhibitor (firocoxib) in the treatment of canine nasal carcinomas

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Introduction

Carcinomas comprise nearly two-thirds of canine nasosinal neoplasms. These tumours are characterized by highly infiltrative growth and low metastatic rate, so treatment is primarily directed at local disease control. Although radiation therapy (RT) has significantly improved prognosis, long-term control is poor, with median survival times of 12 months. Cyclooxygenase-isofom-2 (COX-2) is an inducible enzyme expressed in 71–87% of canine nasal carcinomas and has been linked to tumour growth and angiogenesis. Accordingly, COX-2 inhibition seems rational to improve outcome. EGFR (epidermal growth factor receptor) overexpression in cancer is associated with poor prognosis and may enhance radioresistance. This study aimed to assess the efficacy of the combination of RT and a selective COX-2 inhibitor (firocoxib) in the treatment of canine nasal carcinomas. The prognostic role of COX-2 and EGFR expression was also investigated.

Materials and Methods

Dogs with histologically confirmed and previously untreated nasal carcinoma were randomized to receive 3D conformal RT (5x6 Gy or 10x3 Gy) or the combination of RT and firocoxib (5 mg/kg PO q24h). Patients underwent physical examination at 3-months intervals and were monitored with complete blood count, serum biochemical profile, coagulation parameters and urinalysis to assess firocoxib-related toxicity. CT control studies were also performed to objectively assess the response to therapy. Pet owners were asked to complete monthly a quality of life (QOL) questionnaire. Considered parameters were mobility, interaction, appetite and local pain. For each category, a score of 1 to 3 was assigned, with 3 being the best performance score. Immunohistochemistry (IHC) was carried out on formalin-fixed and paraffin-embedded biopsy samples in order to assess COX-2 and EGFR expression. Immunopositivity was scored as the product of the percentage of positive cells and the intensity of labeling.

Results

Twenty-four dogs (15 females and 9 males) were prospectively enrolled. According to Adam’s modified system, there were 5 stage I, 5 stage II, 3 stage III and 11 stage IV patients. Two dogs had metastases to regional lymph nodes at presentation. The mean follow-up time was 273 days. Median progression free interval (PFI) was 180 days in the RT group (n = 12) and 197 in the RT + firocoxib group (n = 12). Overall survival (OS) was 232 and 346 days, respectively. These differences were not statistically significant. Similarly, response to therapy, as assessed by CT, was not significantly different between the two treatment groups. Metastases to regional lymph nodes were the only significant prognostic factor (OS, P < 0.001). QOL was significantly improved in the RT + firocoxib group (P = 0.026) [Figure 4; Table 1]. No patient experienced firocoxib-related toxicity.

Histologically, there were 12 adenocarcinomas, 4 squamous cell carcinomas, 3 transitional cell carcinomas and 5 undifferentiated carcinomas. COX-2 expression was evaluated in 14 cases and a positive signal was observed in 5 (36%), with a mean score of 3 [Figures 5a-b]. EGFR was expressed in 11 of 13 cases (85%) with a mean score of 7 [Figures 6a-b]. No relation was observed between marker expression and response to therapy.

Conclusions

Firocoxib in combination with RT is safe and improved QOL in dogs with nasal carcinomas. However it did not provide a significant enhancement of PFI and OS, possibly due to the small sample size. Response to therapy was not affected by COX-2 or EGFR expression.

References