ONCOLOGY CHAPTER ABSTRACTS

AN UPDATE ON INTRANASAL NEOPLASIA IN THE DOG: A RETROSPECTIVE EVALUATION OF DEMOGRAPHICS AT PRESENTATION, DIAGNOSIS, AND TREATMENT.

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Background: Intranasal neoplasia comprises approximately 1% of all canine neoplasms, but 10% of cases seen by oncologists.
Aims: To illustrate the demographics, diagnosis, and treatment of Australian dogs with intranasal neoplasia.
Methods: Retrospective analysis of case records of 55 dogs with a high clinical index of suspicion or diagnosis of intranasal neoplasia.
Results: The mean age of patients was 10.4 years. There was no gender predisposition (p=0.106). Staffordshire terrier and Staffordshire crosses seem overrepresented compared to other breeds, at 14.5% (8/55) of cases. The commonest presenting signs were epistaxis (80%, 44/55), other nasal discharge (34.5%, 19/55) and sneezing (58.2%, 32/55). Common physical examination findings were unilaterally reduced to absent nostril airflow (29.3%, 12/41), abnormal upper airway sounds (24.4%, 10/41), and nasal discharge (24.4%, 10/41). As part of diagnostic work-up, 42/55 (76.4%) cases had magnetic resonance imaging or computed tomography, 17 had skull radiography, and 35 had rhinoscopy. 59.5% (25/42) of biopsy-confirmed neoplasms were carcinomas and 28.6% (12/42) were sarcomas. The majority of patients (74.4%, 32/44) were treated symptomatically with analgesic medication, 7 dogs were treated with chemotherapy. Survival data was available for 18 dogs, there was no statistically significant difference in the survival times between dogs treated symptomatically (89 days, n=14) and dogs receiving chemotherapy (132 days, n=4).
Conclusions: The results broadly agree with previous published studies. Staffordshire Terriers/mixes seem overrepresented, perhaps reflecting the larger population. Despite many available treatment options, most clients chose symptomatic care for their dogs. Survival times for dogs treated symptomatically or with chemotherapy were similar.

FUROSEMIDE FOR PREVENTION OF CYCLOPHOSPHAMIDE-ASSOCIATED STERILE HAEMORRHAGIC CYSTITIS IN DOGS RECEIVING METRONOMIC LOW-DOSE ORAL CYCLOPHOSPHAMIDE

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Background: Sterile haemorrhagic cystitis (SHC) is a known risk of cyclophosphamide treatment. Diuresis using furosemide is effective in canines when maximally tolerated doses (MTD) of cyclophosphamide are administered.
Aim: This retrospective study aimed to determine whether concurrent orally administered furosemide decreased the incidence of cyclophosphamide-associated SHC. Secondary aims were to highlight the incidence and identify predisposing factors for SHC in dogs receiving continuous low-dose cyclophosphamide.
Methods: One-hundred and seven dogs treated with continuous low-dose cyclophosphamide between September 2009 and November 2015 had their medical data analysed retrospectively. Information was obtained regarding signalment, diagnosis, use of concurrent piroxicam and/or furosemide, concurrent diseases, bloodwork prior to commencement of metronomic chemotherapy, cyclophosphamide doses administered, adverse effects (including SHC) and outcomes. Populations were not randomised.
Results: 23 dogs (21.5%) developed SHC. Concurrent furosemide administration significantly reduced the likelihood of SHC development (P = 0.005, where SHC was diagnosed in 32.1% of dogs administered cyclophosphamide without furosemide, and 9.8% of dogs administered cyclophosphamide with furosemide). Age, gender, breed, bodyweight, number of cyclophosphamide treatments, piroxicam use, previous or pre-existing disease, and azotaemia or neutropenia prior to onset of clinical signs were not found to be associated with SHC development.
Conclusions: This study demonstrates that furosemide is effective in the prevention of the clinical signs of SHC and its use may be considered when implementing metronomic cyclophosphamide therapy.
LOPP CHEMOTHERAPY AS A FIRST LINE TREATMENT FOR DOGS WITH T-CELL LYMPHOMA

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Background: T-cell phenotype for canine lymphoma has been historically associated with reduced response rates to chemotherapy and remission times compared to B-cell phenotype when treated with CHOP chemotherapy.

Aims: To determine whether a LOPP protocol used for treatment of naive T-cell lymphoma patients improved chemotherapy response rates and disease-free interval (DFI).

Methods: Records were reviewed for patients with naive T-cell lymphoma with full staging having been treated primarily with a modified LOPP protocol to calculate response rates, DFI, OS and to document toxicity of this protocol.

Results: Twenty-seven dogs were identified that fit the inclusion criteria between 2011-2016. The median age was 7.5yrs (range 3-12 years) with 13 neutered males, 11 spayed females and 3 intact male dogs. All dogs were diagnosed with T cell lymphoma based on histopathologic or cytologic lymph node or extra-nodal tissue evaluation and immunophenotyping. 22/27 dogs were diagnosed as having multicentric lymphoma, 2 with cranial mediastinal lymphoma and 2 with hepatic lymphoma. 13/27 were classified as sub-stage b and 8/27 (29%) were hypercalcaemic on presentation. The overall response rate (ORR) of this population was 96% with 24/27 (89%) of dogs assessed as having a CR to LOPP chemotherapy, 2 dogs (7%) had a partial remission and one dog had no response. Of the 26 dogs that had a response to LOPP chemotherapy the median disease free interval was 185 days (range 33-1501 days). The median overall survival time for this study group was 328 days. 18/27 dogs relapsed within the study period and 10 of these dogs received rescue chemotherapy. All deaths in this study were attributable to recurrence of disease.

Conclusions: LOPP chemotherapy for T cell lymphoma is well-tolerated and has an excellent overall response rate but does not significantly improve upon previously reported DFI’s or OS for T cell lymphoma treated with other protocols.
NOVEL ANTIMETASTATIC PROTOCOLS IN CANINE OSTEOSARCOMA – AN UPDATE

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Background: Osteosarcoma (OS) is the most common malignant primary bone tumour of dogs. Effective surgical treatment of local disease and prolongation of survival through adjunctive chemotherapy is often possible. Despite treatment most patients succumb to distant metastases. Currently no effective treatment exists to specifically prevent metastatic disease.

Aims: To investigate the safety and efficacy of auranofin, an inhibitor of thioredoxin reductase 2 (TXNRD2), in the prevention of osteosarcoma metastases.

Methods: Dogs with spontaneously occurring osteosarcoma and without evidence of pulmonary metastases on thoracic imaging, were treated with; amputation, followed by carboplatin (300mg/m² intravenously for 4 treatments at 3 weekly intervals) and auranofin (9mg orally every third day); local radiation therapy (10Gy/7 days for 3 treatments) and auranofin; or amputation followed by auranofin. Serum samples to measure TXNRD2 were obtained prior to starting auranofin and at 3 monthly intervals there-after. Thoracic radiography was performed at 3 monthly intervals until metastases were detected.

Results: 49 dogs were recruited (48 with appendicular osteosarcoma; 40 treated with amputation, carboplatin and auranofin; 6 treated with radiation therapy and auranofin; 2 treated with amputation and auranofin; and 1 dog with primary osteosarcoma of a rib, treated with excision, carboplatin and auranofin). At present insufficient time has passed to determine if survival or time to development of metastasis is significantly different from historical controls.

Conclusion:
Auranofin does not appear to be associated with adverse events when used adjunctively in the management of canine osteosarcoma using the aforementioned dosing regimen. It remains to be seen if there is a significant antimetastatic or survival advantage.
PHASE I/II TRIAL OF AN IMMUNOLOGIC AGAINST CANINE SOFT TISSUE SARCOMA

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Background
CD40 is a surface protein present on antigen presenting cells with ligand on Th cells. Activation with IL-2 leads to increased macrophage activity and B cell activation. A combination of IL-2 and a CD40 agonist showed remarkable benefit against various cancers in mice with regression linked to a neutrophil dominant inflammatory response.

Aims
To prove the safety and efficacy of an intralesional combination of IL-2 and a CD40 agonist in dogs with soft tissue sarcoma.

Methods
Based on information from the mouse studies, an initial dose was determined empirically as probably safe. Doses were increased with each group of 3 having no adverse effects. Each dog was given 6 intralesional injections over 2 weeks before a needle core biopsy 1 and 4 weeks post treatment. This study was approved by the Curtin University Animal Ethics Committee.

Results
At the time of writing, 6 dogs have completed the protocol. One dog was euthanased due to progression of disease with no evidence of necrosis or inflammation. Another dog was euthanased following sepsis 2 weeks post treatment. The majority of dogs have shown necrosis throughout the biopsy with variable inflammation.

Conclusion
Preliminary findings of a phase I/II trial using a combination of our own CD40 and a commercially available IL-2 against canine soft tissue sarcoma have shown no adverse effects but with evidence of necrosis within post-treatment biopsies.

PREVALENCE OF EXON 11 INTERNAL TANDEM DUPLICATIONS IN THE C-KIT PROTO-ONCOGENE IN AUSTRALIAN CANINE MAST CELL TUMOURS

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Background. Testing tumours for C-KIT mutation status is not readily available in Australia. A reasonable proxy for testing might be knowledge of the mutation’s prevalence in tumours from Australian dogs. Aims. To measure the prevalence of C-KIT exon 11 internal tandem duplications (ITDs) in an unbiased sample of Australian canine mast cell tumours (MCTs) and to evaluate relationships between tumour mutation status and commonly used prognostic factors.

Methods. C-KIT exon 11 ITDs were detected by polymerase chain reaction (PCR) in DNA extracted from formalin fixed, paraffin embedded canine MCT blocks from 3 veterinary diagnostic laboratories in Adelaide and Melbourne. Tumours were graded according to both Patnaik and Kiupel systems by board certified anatomical pathologists blinded to PCR results. Relationships between tumour mutation status and prognostic factors were evaluated using a generalised binary logistic regression analysis.

Results: ITDs were identified in 13/74 samples, a prevalence of 17.6% (CI: 8.9%-26.2%). ITDs were detected in 10/18 Patnaik grade III MCTs (55.6%) and 11/22 Kiupel high grade MCTs (50%). Wald chi-square analysis revealed that tumour ITD mutation status is significantly associated with both Patnaik’s and Kiupel’s histologic grading systems (p = 4.8x10^-4 and p = 1.2x10^-4 29 respectively). The presence of the ITDs in MCTs was not associated with signalment, tumour anatomical location or tumour size.

Conclusion: The prevalence of activating ITDs in exon 11 of C-KIT in Australian canine MCTs is similar to the prevalence in overseas canine populations (overall prevalence in Australia approximately 18%). ITDs are more frequently identified in higher grade MCTs.