Oncology

Primary mesenchymal tumours of the thoracic wall: a long-term study of 46 dogs
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A study was undertaken which comprised all dogs with a primary tumour of the thoracic wall which were presented to the University of Cambridge during the period from 1985 to 1998. Other signs included lameness (10 cases), dyspnoea (six), lethargy (three) and coughing (three). Metastasis was identified at presentation in nine dogs, comprising pulmonary (six cases), bronchial lymph node (two) and osseous (three) metastases. The histological types were osteosarcoma (13 cases), chondrosarcoma (13), fibrosarcoma (five), undifferentiated sarcoma (six), haemangiosarcoma (four), myosarcoma (two), chondroma (two) and haemangipiericytoma (one). Surgical resection of the mass was performed in 27 dogs, and reconstruction was achieved by direct closure (eight cases), implantation of polypropylene mesh (12), diaphragmatic advancement (six) and a latissimus dorsi muscle flap (one). Augmentation of the repair with omentum was performed in five dogs. Local recurrence was observed in three dogs at 10 to 12 weeks postoperatively. Fourteen dogs developed metastases at a median of 17 weeks, with spread to the lungs (11 cases), bronchial lymph nodes (one), ilium (one) and heart (one). The median survival time for those animals treated conservatively was five weeks and for those treated surgically, 26 weeks. The median survival time for animals with osteosarcoma was 17 weeks and for fibrosarcoma, 26 weeks. Around half of the animals with chondrosarcoma were alive two years postoperatively. It is concluded that most mesenchymal tumours of the thoracic wall are malignant. Conservative treatment is associated with a poor prognosis in such cases. Chest wall resection results in a prolonged survival time, particularly for chondrosarcomas, and is not associated with significant complications.

Radical surgical resection of the canine maxilla as treatment for squamous cell carcinoma of the nasal planum
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The extent of maxillectomy required to gain tumour-free margins has often been considered to be the limiting factor in choosing surgery as the treatment modality for squamous cell carcinoma (SCC) of the nasal planum. The authors describe the surgery and outcome following radical resection of the canine maxilla for invasive SCC of the nasal planum. Two dogs were presented with confirmed SCCs of the nasal planum and rostral maxilla – tumour stages T4N0M0. Computed tomographic scans showed tumour extension to just caudal to the left canine in one, and level with the apex of the left canine in the other. Surgery involved removal of the maxilla to the level of the 2nd premolar bilaterally in one dog, and the 3rd premolar bilaterally in the other. Surgical time was approximately 75 minutes. Intraoperative problems were limited to blood loss. Tumour-free margins were obtained in both cases. Immediate postoperative problems were pain, inappetence and also soiling of the remaining maxilla with discharge, mucus and food material. One dog suffered irritation and dermatitis of the area and progressive stenosis of the rostral airway orifice. There was no recurrence of tumour at 25 and two months follow-up, respectively. Both owners indicated that they would be willing to repeat the procedure on another dog if required. In conclusion, radical maxillectomy to the level of the 2nd or 3rd premolar for SCC of the nasal planum and rostral maxilla was well tolerated by two dogs and acceptable to owners.

Evaluation of single-agent doxorubicin as rescue chemotherapy for relapsing canine lymphoma cases
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The aim of this retrospective study was to evaluate doxorubicin as single-agent rescue therapy for canine lymphoma cases refractory to cyclophosphamide (C), vincristine (O), prednisolone (P) and cytosine arabinoside (A). Twenty-eight dogs were evaluated: 19 were previously treated with low-dose COP, eight with COAP and one with high-dose COP. Additional drugs were given in some cases: melphalan (six dogs), aspiraginase (four dogs) and vinblastine (two dogs). Doxorubicin was administered at 30 mg/m² intravenously every 21 days (up to seven treatments). Two cases received epirubicin, a close structural analogue of doxorubicin, as part of their schedule. The overall response rate was lower following doxorubicin therapy than for the primary treatment (46.4 per cent versus 96 per cent). The overall median actuarial survival from day 1 of doxorubicin treatment for 19 of 28 dogs which received no other drugs was 31 days. Complete responses were achieved in five of 28 cases (17.8 per cent), partial responses in eight cases (28.6 per cent) and no response in 15 cases (53.6 per cent). For the five complete responses, the median remission time was 133 days (including one dog in remission at the time of writing, at 140 days). Toxic effects included vomiting (three dogs), diarrhoea (three), anorexia (two), mild thrombocytopenia (four) and cardiac arrhythmias (two). The results of this study show that doxorubicin has limited value as a rescue agent for relapsed lymphoma cases which are refractory to C, O, P and A.

Escherichia coli nitroreductase/CB1954: in vitro studies into a potential system for feline cancer gene therapy
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Prodrug activating systems have received a great deal of attention in cancer gene therapy research. Target cells are transduced with the gene for an enzyme, which is then expressed. A prodrug is administered systemically, which is converted from its non-toxic to its cytotoxic form by the enzyme expressed in target cells. The most commonly used enzyme/prodrug combinations – herpes simplex virus thymidine kinase/ganciclovir and cytosome deaminase/5-fluorocytosine (5-FU) – are unsuitable for feline use because of the inherent toxicities of the prodrug (ganciclovir) or active metabolites (5-FU). Recently, the Escherichia coli nitroreductase (NTR)/CB1954 system has emerged as a useful combination in other species. The aim of the present study was to identify a suitable prodrug activating system for feline cancer gene therapy. Feline kidney (CRFK) cells were transfected with plasmids encoding the gene for NTR. Expressd enzyme was detected by SDS-PAGE followed by Western blotting. Further transfections were carried out, then cells were treated with CB1954 and toxicity was assessed. Feline cells expressed NTR without toxicity. The expressed enzyme was able to activate CB1954, resulting in cytototoxicity to both transformed and adjacent cells in vitro, confirming the bioactivity of the enzyme and the presence of a bystander effect. In the absence of NTR, CB1954 was non-toxic to feline cells in vitro, suggesting the absence of endogenous enzymes capable of significantly activating the prodrug. These preliminary results suggest that E. coli NTR may be a useful system for feline cancer gene therapy. Evaluation of the system in other feline cell lines in vitro is warranted, and toxicity trials of CB1954 should be considered if the results of further in vitro work are favourable. (CB1954 was kindly donated by Dr Peter Harris, Cobra Therapeutics, Keele University Science Park.)
Paraneoplastic hypereosinophilia in a cat with T-cell lymphosarcoma

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As a paraneoplastic syndrome in the cat, hyper eosinophilia, characterised by peripheral and tissue eosinophilia, is often considered a marker for mast cell neoplasia. In contrast, the authors have documented hyper eosinophilia in a cat with a diffuse, alimentary, CD3+ T-cell lymphosarcoma. A 10-year-old neutered, female, domestic shorthaired cat was presented with a two-month history of weight loss and small bowel diarrhoea. On abdominal palpation, mesenteric lymphadenopathy and markedly thickened intestines were noted. A peripheral eosinophilia was detected on haematological analysis. Cytology of fine needle aspirates from the enlarged lymph nodes demonstrated large numbers of eosinophils. At exploratory laparotomy, the small intestine was diffusely thickened and friable, and several plaque-like masses arose from its mesenteric border. An abdominal effusion was present, with 95% per cent of nucleated cells being eosinophils. Histopathology of the mesenteric lymph node showed a severe eosinophilic lymphadenitis. Immunostaining for feline coronavirus antigen was negative. The cat did not respond to oral prednisolone and was euthanased. Eosinophil infiltration of intestinal walls and mesenteric lymph nodes was detected on histopathology. Large aggregates of neoplastic round cells, present in the intestine, stomach and lymph node, were identified as CD3+ T lymphocytes. Immunostaining may be necessary to distinguish lymphosarcoma from mast cell neoplasia. Lymphosarcoma should be considered an important differential diagnosis for eosinophilia in the cat. The mechanism of eosinophil recruitment is unknown, but may be secondary to the production of interleukin-5 by neoplastic lymphocytes.

Dendritic cell immunisation for the treatment of canine malignant melanoma

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Canine oral malignant melanoma is an aggressive neoplastic disease. Although radiotherapy has been used successfully for the treatment of the primary tumour, this fails to influence the natural progression of metastatic disease. It has been proposed that a lack of normal immunity to neoplastic cells is due to a deficiency in the presentation of tumour antigens by dendritic cells (DCs). Therefore, human patients have been treated by loading DCs with melanoma antigens in vitro, and injecting these cells to stimulate tumour-specific immunity. The aim of this study was to generate blood-derived DCs from canine melanoma patients and to assess whether DC immunisation can be used for the treatment of canine malignant melanoma. Two dogs with oral malignant melanoma were recruited for a preliminary study. Peripheral blood mononuclear cells were isolated and cultured with recombinant canine GM-CSF and interleukin-4 (Heska, CO, USA). The resulting DCs from patient 1 demonstrated a typical dendritic morphology and were CD11c+, MHC Class II+ and CD80/86+ by flow cytometry. In patient 2, whole tumour lysate was added during culture and 106 DCs were injected on three occasions. DC immunisation was well tolerated by the patient and no adverse effects had been seen up to the time of writing. This preliminary work demonstrates that DC immunisation is feasible in dogs. Future work will determine whether this strategy can stimulate tumour-specific immune responses and whether DC immunisation can prevent, or at least retard, the progression of metastatic disease in canine melanoma patients.

Myelodysplastic syndrome in a feline leukaemia virus-negative cat

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Myelodysplastic syndromes (MDSs) are characterised by peripheral cytopenias with hyperplastic and dysplastic changes in non-lymphoid bone marrow cell lines. In the cat, MDS is considered to be a feline leukaemia virus (FeLV)-related disease. The authors present clinical, haematological, serological, biochemical, histological and immunohistological findings from a case of MDS which was negative for FeLV p27 antigenaemia on repeated testing. A two-year-old neutered, female, domestic shorthaired cat was presented with a two-month history of inappetence, lethargy and weight loss. Physical examination revealed cachexia, icterus, pyrexia, tachycardia, peripheral lymphadenopathy and splenomegaly. A severe, poorly regenerative, haemolytic anaemia (packed cell volume 12 per cent) was detected and thrombocytopenia developed subsequently. Parasitaemia was not detected on sequential blood smears. Autoagglutination of washed erythrocytes precluded blood typing or cross-matching. Therefore, the risks associated with bone marrow aspiration were considered excessive. Response to antimicrobial and immunosuppressive therapy was minimal and the cat died seven weeks after presentation. On histopathology, the bone marrow was hypercellular, with dysplasia in erythroid and megakaryocytic lines. The proportions of CD3+, CD45R+ and MAC 387+ cells in the bone marrow were compared with those from a group of 72-week-old specific-pathogen-free cats. A diagnosis of MDS was made. It is concluded that underlying MDS should be included in the differential diagnosis of haematologic anaemia, even in the absence of FeLV antigenaemia.