



### Canine appendicular osteosarcoma

Erik Teske, DVM, PhD, Dip ECVIM-CA

Dept Clin Scie Comp Anim, Utrecht University, The Netherlands

e.teske@uu.nl

Osteosarcoma is a malignant spindle cell tumour, characterized by the direct formation of bone or osteoid tissue by the tumour cells. It is the most common bone tumour in the dog with a reported incidence of 5.5-6.5/100.000 dogs. The majority (>75%) are appendicular, while the others are in the flat bones, the axial skeleton or extra skeletal (e.g. mammary gland).

Appendicular osteosarcomas are seen more often in large or giant sized breeds. Less than 5% of the osteosarcomas are seen in breeds <15kg. In a recent publication of Nationwide Pet Insurance in the USA (2016) several giant breeds were indicated with an increased risk with the highest prevalence of 7.3% reported for the Irish Wolfhound. Also the Greyhound was high on the list with a prevalence 5.5%, but this might be special for countries in which Greyhounds are used for racing, as most of these dogs were old racing dogs. Repetitive micro-trauma might be responsible for this. Other physical factors suspected for being responsible for osteosarcoma are metallic implants and radiation therapy. There have been several molecular and genetic factors associated with osteosarcoma. Some of them are retinoblastoma (Rb), p53, c-Met, and the growth factors: GH, IGF-I, HGF, and angiogenic factors (e.g. VEGF). The median age for dogs with osteosarcomas is 6-8 years, thereby more a disease for middle aged dogs than old dogs. Although there is no sex difference neutered dogs of several breeds are reported to have a higher risk (Odds Ratio for males 1.4, for females 1.9). Rottweiler dogs with an overall reported incidence of osteosarcoma of 12.6% have a 3-4x higher risk when neutered before one-year of age. After that the risk factor becomes lower.

The tumour is typically located “Away from elbow”, i.e. proximal humerus and distal radius, and “Around knee”, i.e. distal femur and proximal tibia. The front legs are affected twice as often as the hind legs. Dogs with appendicular osteosarcomas usually are presented with a history of lameness and swelling at the primary site. There might be a history of mild trauma prior to the onset of lameness. Acute and severe lameness is often associated with pathologic fractures. Although the definitive diagnosis has to be made by the pathologist the location of the tumour and the radiographic picture can already be very suggestive. Typical characteristics seen on the X-ray are the mixed appearance of osteolysis and proliferation, the Sunburst appearance of the proliferation (palisading pattern perpendicular or radiating from the axis of the cortex), Codman’s triangle (elevation of the periost and deposits of new bone in a triangular form), and the presence of pulmonary metastasis (although only visible in 5-15% at presentation). Histological biopsies with a Jamshidi needle or Michele trephine can give a more accurate diagnosis although histological confirmation of the whole tumour after surgery is still needed. In some instances an elevation of serum alkaline phosphatase can be seen due to a rise of the bone isoenzyme. This has been associated with a poorer prognosis in several studies.

Osteosarcoma is an highly metastatic tumour. In more than 90% metastases are present at the time of diagnosis leading to an one-year survival rate of 10% after amputation. The tumour metastasizes by haematogenous routes (lymph node metastases are extremely rare) and pulmonary metastases are most common. Bone metastases can also occur. Additional bone scintigraphy and/or CT scan are therefore also indicated.

Histologic classification is based on type and amount of matrix and characteristics of cells. Several different subtypes can be seen: Osteoblastic, chondroblastic, fibroblastic, poorly differentiated, and telangiectatic (a vascular subtype). Osteoblastic types are considered to be more aggressive than fibroblastic subtypes. Probably grading is more important than type. Younger dogs have higher grade tumours, and distal tumours also have higher grade, while cranial tumours more often have a lower grade tumour.

Several treatment options are available, although euthanasia should also be considered as a kind alternative. Chemotherapy is only effective in minimal tumour load situations and radiotherapy will only stabilize the tumour for some period but will not definitely kill the tumour. Therefore surgery is the primarily treatment options. The most radical form is of course leg amputation. This will lead to a good local control with removal of tumour and pain, will have a median survival of 4-6 months, and in most cases of very good quality of life. Limb-sparing removal of the tumour and implantation of an allograft can be considered if the tumour is located in the front leg, does not affect more than 50% of the bone, the dog has an otherwise good health, and no pathological fractures are present. All kind of different implants have been used. Eighty per cent of the limb spared OSA-patients experience a good to excellent limb function. Complications recorded are fractures 10%, implant loosening 10%, recurrence of tumour 22% and infection rates of 31-68%. The presence of infections of the implant is, however, in some studies associated with prolonged survival, most likely due to a-specific stimulation of immune system.



# COMPANION ANIMAL

## SURGICAL ONCOLOGY

Adjuvant chemotherapy will further increase median survival up to almost one year. Although cisplatin is the gold standard with reported one-year survival rate of 40-45% it is hardly been used anymore. This due to its high nephrotoxicity, necessitating pre- and post-chemotherapy infusions. Routine adjuvant chemotherapy consists of carboplatin (300mg/m<sup>2</sup>) every three weeks for six cycles with one-year survival rates of 35-38%. Six cycles of alternating doxorubicin and carboplatin resulted in significant poorer results. The following criteria have been identified as independent prognostic indicators for survival: Histologic grade, serum Alkaline Phosphatase and location tumour (distal radius better prognosis).

Radiotherapy is used as a palliation treatment. It will induce necrosis and delays tumour growth. It is primarily used to treat osteolytic bone pain. It is usually delivered during 2-4 fractions with 6-10 Gy. Median time to improvement in limb function after radiation treatment has been reported at 11 to 15 days.

The use of aminobisphosphonates is questionable. They induce osteoclast apoptosis, thereby reducing pain associated with malignant osteolysis. However, conflicting results have been obtained in different clinical trials. In a double-blind placebo controlled study combined with radiotherapy the administration of aminobisphosphonates was safe, but did not lead to improvement of pain alleviation.

Recent studies with tyrosine kinase inhibitor in dogs with metastasized osteosarcoma did not prove any clinical benefit.