

# Canine Osteosarcoma: From Diagnosis to Treatment

Conor McNeill, DVM, DACVIM  
Hope Advanced Veterinary Center  
Vienna, VA

Osteosarcoma (OSA) is the most common primary bone tumor in dogs. 85% of all primary bone tumors in dogs are OSA. The tumor is of mesenchymal origin and is formed in the metaphyses of the bone. There are 2 forms of OSA called appendicular and axial OSA. Appendicular OSA originates on the long bones (limbs). It behaves locally invasive and is considered highly metastatic. The most common metastatic sites are lung tissue and other bones. Appendicular OSA occurs more frequently in large breed dogs and increased weight and height are considered risk factors for OSA. Previous radiation, metallic bone implants and fractures have been shown to predispose to developing OSA later in life. Tumors can originate in any bone, but the distal radius and proximal humerus are much more common than other sites.

Axial OSA is a bone tumor of the flat bones, such as a mandible, maxilla and pelvis. Axial locations are less common than appendicular tumors, but make up about 25% of all canine OSA. Axial OSA is more common in small breeds (<15 kg). The mean age at presentation is about 7-8 years. They generally do not metastasize as frequently as appendicular OSA. However, rib tumors are an exception as these tumors are generally aggressive. 11% have metastasis at presentation and general prognosis is only about 4-5 months from diagnosis.

## Diagnosics

The physical exam findings and history of lameness and swelling will most often show where the bone tumor is located. There can be more than one tumor. Radiographs, nuclear scintigraphy, CT scan and MRI images can help detect the primary bone lesion but also help search for possible (pulmonary or bone) metastatic lesions.

On radiographs, the cortical bone loss, 'sunburst effect' and 'Codman's triangle' are considered classic changes to the bone suggesting OSA. Differentials to consider include fungal osteomyelitis, bacterial osteomyelitis, bone cysts and metastatic neoplasia. With nuclear scintigraphy, OSA cells will cause a patchy pattern of intense isotope uptake which will show as a marked distortion of bony outline and a moderately defined scintigraphic margin. However, nuclear scintigraphy and radiography have been reported to overestimate tumor extent. CT and MRI can also overestimate the tumor extent (when compared to histopathology). When MRI, CT, nuclear scintigraphy, and radiographs were compared to histopathology, MRI was found to be most accurate in evaluating tumor extent.

Three view chest radiographs are recommended to stage for pulmonary metastasis prior to any treatment. 90% of dogs have microscopic metastatic disease to their lungs at their initial diagnosis. A recent report showed that CT is more sensitive than routine radiographs at detecting pulmonary metastasis, particularly in large breed dogs. In dogs with pulmonary nodules detected on a CT scan, only 81% of these also had their nodules found on routine radiographs.

Fine needle aspirate (FNA) can be performed 'blindly' or ultrasound guided. FNA are increasingly used for initial diagnosis. OSA was accurately diagnosed in 85% and 95% of FNA and Core aspirate cytology, respectively. 'Alkaline phosphatase' stains can be used to aid in the differentiation of osteosarcoma on cytology samples. A positive stain turns grey/ black and is highly sensitive (100%), and very specific (89%). However, other mesenchymal tumors of the bone can be difficult to distinguish from the aspirate sample. A biopsy is still considered the gold standard to diagnose OSA. Jamshidi needles are 92% accurate, compared to trephine needles (94% accurate).

## Prognostic markers

For canine OSA, there are several known prognostic factors that can be useful to predict expected outcome: Negative prognostic indicators (which will have a negative impact on outcome) include a diagnosis age less than 7 years or older than 10 years of age; a large tumor; one that is located on the proximal humerus; a high tumor grade (III); increased serum Alkaline Phosphatase on bloodwork before surgery and remaining high a month after surgery; high Cox-2 expression in the tumor; draining lymph node involvement (stage 3).

## Treatment

The recommended treatment for OSA remains surgery (amputation or limb-spare) followed by chemotherapy. Despite aggressive treatment approaches, most dogs die within 1 to 2 years due to metastatic disease. Other surgical considerations include pulmonary metastatectomy, bone transport osteogenesis, and ulnar transposition

### Surgery

For amputation, it is important to prepare the owner well about what their pet's life will be like after surgery. Amputation is the most aggressive method of surgery, but also the most effective for pain control and guarantees complete removal of the primary tumor.

Median survival times for dogs following amputation surgery are generally only 4-5 months as dogs usually succumb to their pulmonary metastatic disease. Survival times with limb-sparing surgery are similar to amputation alone. Limb-sparing surgeries often result in good function of the limb and dogs are near normal weight bearing within a few weeks of surgery. Not all tumor sites are amenable to limb-sparing surgeries so this option is not for every patient. Complications to prepare the owner for are possible bone resorption, implant failure, infection at the surgery site and tumor recurrence ('incomplete margins'). Dogs that developed infections in their wounds often had an improved outcome. This is thought to have been from immune mediated attack of the tumor sites from the surrounding infection.

Surgery followed by adjuvant chemotherapy significantly increases the 1- and 2-year survival rates, with 40% of dogs alive at 1 year, and 20% of dogs alive at 2 years.

### **Chemotherapy**

With amputation followed by chemotherapy, the median survival times range from approximately 10-14 months. Chemotherapy is most effective at the maximum tolerable dose. In theory, multi-drug chemotherapy protocols are considered superior to single agent treatments. This is due to a heterogeneous tumor population and possible intrinsic resistance to one chemotherapeutic agent. The three most effective drugs to date are doxorubicin, cisplatin and carboplatin. The optimal treatment is yet to be determined. One protocol has not been shown to be convincingly superior to others. Currently there are several new drugs and treatment being investigated, including an oral formulation of a platinum drug (satraplatin), palliative control of metastatic lung lesion with tocenarib phosphate, metronomic therapy with cyclophosphamide and piroxicam and several other small molecule inhibitors. Current research is ongoing to determine the efficacy and clinical application of an osteosarcoma vaccine that targets HER-2 expressed by the cancer cells. Preliminary results are very promising, but this product is currently not yet commercially available but hopefully will be an option for patients in the near future.

### **Radiation therapy**

Palliative radiation is very effective at treating pain from the tumor in the affected limb. The goal of palliation is to reduce local inflammation and pain caused by the tumor which will improve the patient's quality of life. 50-92% of dogs treated were reported to have a response to treatment. The median time for onset of response is less than 2 weeks. The median duration of response was 2-4 months. Better responses were seen if less than half of the bone was involved and if the tumor was located in proximal humerus. Prognosis with radiation alone is about 4-6 months on average. Adding chemotherapy can extend outcome in some dogs from 3 to 11 months.

Stereotactic radiosurgery is a highly specialized method of delivering radiation therapy to the bone tumor. The entire treatment dose is delivered as a single (or a few) treatment using multiple non-coplanar beams that are stereotactically focused in the target. This gives a greater potential biological effect and minimizes the damage to healthy tissues. Fewer anesthetic episodes are needed than with conventional radiation. This treatment is offered at a few larger clinics in the country, and is more expensive than regular radiation. It is an option for clients willing to travel.

### **Palliative options**

Chemotherapy can be given as medical palliation to address the cancer cells in the tumor but is less effective than in the adjuvant (post-surgical) setting. For pain medication alone, NSAIDs often give inadequate pain control. Opioids are more potent analgesics, but the options are limited for at home use (codeine). Tramadol, Gabapentin and Amantadine are good options to combine with NSAIDs to optimize the pain control for the patient and improve their quality of life.

Bisphosphonates, such as pamidronate, are analogs of the endogenous pyrophosphate. The method of action for these drugs is not fully understood. They inhibit farnesyl diphosphate synthase, which is a key enzyme in mevalonate pathway and is essential for normal cell function and survival. Effects of bisphosphonates on tumors include induction of apoptosis, and inhibition of proliferation, tumor cell adhesion and invasion, angiogenesis and bone metastasis. Unlike humans, in dogs, oral administration has minimal bioavailability and intravenous administration is more effective. Research has shown that these drugs give minimal pain control. We currently use them in the palliative setting to help with bone matrix strengthening.

Chemoembolization embolizes the arteries supplying blood to a tumor. The effect is an increase in the local concentration of the chemotherapy drug and dwell time of the drug. This in turn increases tumor ischemia and minimizes systemic toxic effects. This treatment is recommended only for palliation of otherwise inoperable lesions. It is a highly specialized technique with only a few centers offering it for patients.

### **Axial tumors**

For axial tumors, treatment depends very much on location as surgery is often very difficult. For tumors located in the mandible or maxilla, surgical resection is possible. For those on vertebrae, this is more challenging. Axillary OSA tumors are less likely to spread. Local recurrence of the tumor is usually a problem before metastatic tumors arise. The exception to this is rib OSA, which has a high metastatic risk. Due to the limitations for treatment, canine axial has an average prognosis of only 4-5 months.