



THE PATHOLOGIST'S CORNER

by Dr. Marilène Paquet

Canine Osteosarcoma Under The Microscope

What is an osteosarcoma?

An osteosarcoma (OSA) is a malignant primary bone tumour. The name comes from two words: “osteo,” referring to bone and “sarcoma,” referring to a malignant tumour originating from connective tissues. The term “malignant” means that it is a tumour with the potential to invade the surrounding tissues and disseminate to distant lymph nodes and organs. This is a neoplasm diagnosed with high frequency in large and giant canine breeds such as Irish Wolfhounds, Great Danes and Rottweilers. It is also occasionally seen in small breeds of dogs, as well as in cats but is fairly rare in other domestic species and in humans¹. The term “primary osteosarcoma” refers to a group of malignant tumours that originates from the bone tissue itself. Bone is a naturally complex tissue composed of several cell types that can all contribute to the tumorigenic process. In general, the common element in all types of osteosarcoma is a variable production of bone matrix, which can show different degrees of calcification (and hardness).

What are the risk factors involved?

As you might know, osteosarcoma (OSA) is the number one primary bone tumour in dogs and is fairly common in several breeds. In fact, according to a Norwegian study, OSA have an incidence of 10 to 50 times higher in canine than in humans with 80% of the tumours diagnosed in dogs older than 7 years. When it comes to risk factors for OSA, size definitely matters! The size and height of canines influence the disease predispositions with large dogs (25 to 45 kg) and giant dogs (> 45 kg) being the most frequently afflicted. The Irish Wolfhound, the largest of the group, has the highest prevalence for the disease and one of the lowest median age of onset (6,6 years of age). Interestingly, there is a stronger association with the size of the dog than

with any specific breed². These findings highlight that the selective breeding for long legs and large size in any breed, increases the risk for osteosarcoma by selecting risk alleles in the dog's genome³. However, it's not just about genes and heritability since no single gene is responsible for the disease in dogs. Several regions in the genome appear to be involved making OSA a heritable disease but with additional complex influences from factors such as epigenetics, replicative mutations, environment, hormones and nutrition during growth among others^{4,5}. As an example, large dogs with long legs have a prolong growth period. Their growth plates are susceptible longer to the forces of heavy weight bearing and shear stress. In addition, the longer the growth period, the longer the rapidly proliferating cells in growth plates will be exposed to DNA damage and replication errors¹. Since male dogs are usually larger and heavier than females, past studies showed that OSA were more frequent in males than in females however recent data suggest a rather equal sex distribution^{1,6}. Some studies suggested that neutered male dogs had higher risks for the disease however, a closer look at these studies showed several bias and confounding factors limiting the power of the finding⁴.

What are the main clinical characteristics?

In large dogs (as in children), OSA have a predilection for the metaphysis of long bones¹. These bone regions (extremities close to the joint) transfer the weight-bearing forces from the joint itself to the diaphysis (mid section of long bone) and are frequently under strains. In growing animals, the metaphysis is also the site for the growth plates in which several specialized cells will allow the bone to form and elongate until maturity. Since dogs carry 60% of their body mass on their front legs and 40% on their back legs while standing, it's not

surprising that the distal radius with 24% of the lesions (close to the wrist) and proximal humerus with 26% of the lesions (close to the shoulder) are the two most common locations for OSA in large dogs. Other frequent locations are the distal femur and proximal tibia (close to the knee joint) on the back legs. The typical presentation will be swelling and pain to the touch. The dog will have a history of lameness that progresses from mild and intermittent to persistent and severe². When the affected limb is non-weight bearing, it is usually associated with a “pathological fracture.” These fractures occur through the weakened diseased bone and are known to occur in about 38% of the cases in dogs. A definitive clinical feature of OSA in dogs is the high rate of metastases to distant sites (mostly the lungs). Although less than 15% of canines have radiographic evidence of metastases at the time of diagnosis, 85% will develop metastases despite an aggressive treatment of the primary tumour^{1,6}. This finding suggests that most dogs have very small metastases (micrometastases) at the time of diagnosis.

What should you know about diagnosing canine OSA?

OSA in large dogs are straightforward to diagnose from the clinical point of view. The disease has a high frequency in some large and giant breeds and the locations and clinical signs (as described above) are well known by veterinarians. The radiographic findings show bone loss (w/o a pathological fracture) with atypical soft tissue proliferation/swelling, abnormal bone deposition w/o calcification. To confirm the tumorous process, a biopsy or a fine needle aspirate is required to demonstrate the presence of cancerous cells. Thoracic radiographs and computed tomography (CT) are useful to evaluate metastatic spread to the lungs. Interestingly, a study showed that the CT was superior to the radiographs to pinpoint micrometastases².

A word on canine OSA treatment

To this day, limb amputation remains the conventional treatment for appendicular OSA. The limb with the tumour is removed as well as draining lymph nodes. The pathologist can then determine the tumour grade, the cleanliness of the margins and the presence or absence of metastases in the regional lymph nodes. Limb amputation prevents the risk of pathological fractures and alleviates pain. This proce-

dure might sound dramatic but is generally well tolerated by canines and gives them back a good quality of life. Nevertheless, surgery alone is only palliative since a large proportion of patients will develop detectable metastases within 6 months to a year. Studies showed that adjuvant chemotherapy when associated with surgery and/or radiotherapy greatly improve survival^{2,6}. On a final note, a large number of dogs will be diagnosed with OSA this year. The therapy of the future relies on a better understanding of the genetics involved in OSA, the development of targeted therapies with fewer side effects and the discovery of biomarkers that could help in the diagnosis or the monitoring of the clinical response to a particular treatment. Since canine OSA parallel human OSA in several aspects including genetics, risk factors and tumour behaviour, any advance in scientific knowledge, diagnostic procedures and treatments for one is a gain for all.

References:

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