

Osteosarcoma: The Nemesis of Large Breed Dogs

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To start, what is an Osteosarcoma?

Osteosarcoma is a cancer of bone, which has its origin in the bone forming cells called osteoblasts.

What causes these cells to become cancerous?

A number of reasons have been found. However, essentially osteosarcoma is a genetic disease and the events that lead up to the cell becoming cancerous are related to changes in the genetic structure of the cell. These changes can be due to inherited causes (e.g. certain large breeds of dogs are prone to this cancer), environmental causes (e.g. radiation), and biological causes (e.g. viruses).

Is it malignant?

By malignant we mean cancer spreading to the local gland and /or other organs. The osteosarcoma is considered a highly malignant cancer with about 100% mortality if not treated. The osteosarcoma cells have genetic changes, which allow them to escape from the "mother cancer" and invade distant sites. The cancer cells use enzymes called "matrix metalloproteinase's" or MMP's to invade the healthy tissue. These enzyme digest membranes and connective tissue allowing invasion. The cells also have the ability when they reach a certain size to recruit blood vessels to help them grow bigger; we call this "angiogenesis." Most deaths from malignant cancer, even though the "mother cancer" is treated successfully, are because of spread to distant organs. In the case of osteosarcoma, that organ is the lung; other organs can also be affected but less often.

What breeds are affected and what is the risk to my dog?

We use three terms to describe the occurrence of a cancer, these are: incidence, prevalence and risk. By incidence, we mean the number of new cases occurring during a specific time interval such as one year. By prevalence, we mean the total number instances of old or new cases in one year. By risk, we mean a risk factor that increases the likely hood of osteosarcoma. We know from research that large and giant breeds of dogs weighing greater than 40kg (88lbs) accounted for 29% of osteosarcoma cases. Dogs less than 15kgs account for less than 5% cases. It is obvious from the data that weight is certainly a risk factor for developing osteosarcoma.

Breeds	% Incidence for the breed
Irish Wolfhound	4.88
Rottweiler	4.80
Greyhound	4.27
Great Dane	4.26
Irish Setter	3.95
Samoyed	3.39
Akita	1.57
Doberman Pinscher	1.47
Siberian Husky	1.38
Golden Retriever	1.11
Labrador Retriever	0.94
Basset Hound	0.79
Australian Shepherd Dog	0.46
Mixed Breed	0.44
Boxer	0.32

Another obvious risk factor would be breed; Table 1 lists the dogs at risk although weight appears to be more important. Other less important risk factors include: surgical implants, chronic bone infections. The incidence in the USA is estimated to be about 8,000 new cases per year. This could be higher as most are not reported. True prevalence is unknown.

How will I know my dog has osteosarcoma and where will it most likely occur?

The most important sign is bone pain. If the legs are affected the early sign are generally lameness, this can even precede radiographic changes of osteosarcoma. Follow-up X-rays for a non-resolving lameness are very important especially in large breeds.

Approximately 75% of cancers occur on the long bones of the legs. In the back leg, the most common sites are around the knee (stifle), and some around the hock. In the front leg, the shoulder area (proximal humerus) and the distal radius (corresponds to the wrist area in humans) are the most common sites. The tumor in the more advanced stage is recognized as a swelling over the affected area that is painful and feels “hot to touch”. To make the diagnosis, veterinarians need to do radiographs (x-rays) of the affected bone and the lungs. The cancer looks very typical on radiographs, but to confirm the diagnosis the vet must do a biopsy of the tumor. At the University of Florida, we typically use a biopsy needle called a Jamshidi. The biopsy does require an anesthetic as the procedure is painful and require good pain medication at this time as the cancer pain seems to flare up after the biopsy. The diagnosis is then confirmed by a pathologist. It is not uncommon for a biopsy to come back negative and the biopsy needs to be redone. It is a delicate balancing act between taking enough tissue for diagnosis, but not so much that the bone is weakened

¹ Data compiled from 1996-2004 case records seen at the UF VMTH and analyzed by Julie Rosenberger (Class of 2007) and Dr Cynda Crawford, University of Florida

further. X-rays of the lungs are vital to identify spread of the cancer to the organ, caution should be noted here as x-rays only start picking up spread after the cancers reach a certain size (about 2mm in diameter).

So you have given me this terrible news what are the treatment options for my dog?

Table 2		
Treatment	% Alive 1 year	% Alive 2 years
Amputation <u>without</u> chemotherapy	10%	
Amputation with chemotherapy	30-62%	7-21%
Limb sparing with chemotherapy	63%	
Radiation (SRS) and chemotherapy (UF) ²	50%	38%

When we treat osteosarcoma in our pets we generally have two goals in mind. The first, which is more by way of a question, can the cancer be cured? Generally, most malignant cancers in dogs cannot be cured and osteosarcoma is no exception. If that is the case, our next step would be to provide palliative care. With osteosarcoma we generally focus on two aspects of palliative care, the first being pain control. Effective treatment in the early stages of the cancer is to put the dog on an anti-inflammatory drug such as carprofen, deracoxib, or piroxicam, or other non-steroidal anti-inflammatory. These drugs should not be combined with cortisone (prednisone) or other steroids as they can lead to severe gastrointestinal bleeding. At the time of biopsy, additional narcotic painkillers are also needed. Probably the most effective method in controlling pain is to amputate the leg. In a sizable number of cases this choice is not exercised because of medical and/or owners preferences. In that case what we do radiation treatment of the primary cancer, or limb sparing surgery (replacing the affected bone with a surgical implant or prosthesis), or a radiopharmaceutical treatment. Owners are also justified in considering euthanasia as osteosarcoma is a very painful cancer and cure is unlikely.

The second aspect of palliative care is to treat the primary cancer and suppress spread. A number of the treatments for pain (e.g. limb sparing, amputation and radiation) form the basis of primary tumor control. Choices for treatment must take into account cost versus benefit, stage of the cancer, owners concerns, and expertise of the clinician. Table 2 gives a list of survivals for various treatment types. The purpose of chemotherapy adding to primary treatment such as surgery or radiation is to control distant spread, which in most cases is to the lungs. Chemotherapy is only moderately effective in delaying the spread of the cancer.

What's in the pipeline for new treatments?

At the University of Florida, we are continuing our research in stereotactic radiosurgery (SRS), see Table 2. It promises to be a viable alternative to amputation. We have found that pain control is good and that long-term control of the primary tumor is possible. Other areas of research include blocking MMP's and angiogenesis to slow down secondary spread of the cancer to vital organs such as the lung. In addition the use of

² Early not published data

bisphosphonates (human drugs used to treat osteoporosis) seem promising in controlling bone pain and preventing spread of the cancer. Arguably, the most important development will be an immune stimulant or vaccine that will help the body block the spread of the cancer to vital organs.