



Pacific Tide

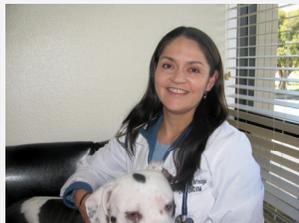
An informational monthly newsletter

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Author of the month:



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Dr. Arteaga received a B.S in Biochemistry and Environmental Toxicology from UCLA. She received her DVM from Cornell University Veterinary Medical School in 2003. Dr. Arteaga did her internship in Medicine and her residency in Oncology at Animal Medical Center in New York City and obtained Board Certification from the American College of Veterinary Internal Medicine, (Oncology) in 2009. Dr. Arteaga continues to speak locally and nationally and participate in clinical trials including the USDA DNA Melanoma vaccine with Memorial Sloan Kettering. She introduced emerging immuno and targeted therapies including the melanoma vaccine, palladia, metronomic and bisphosphanate therapy to the Monterey community. Her goal is to educate, collaborate with veterinarians and owners and offer a full spectrum of treatment with her patients living normal lives with cancer. Dr. Arteaga is available for consultations Monday through Friday and look for her most recent scientific article, "Feline Colonic Adenocarcinoma with Carboplatin" in the upcoming Journal of American Animal Hospital.

Canine Osteosarcoma

I wrote this article 3 years ago at a time when the "ceiling" for osteosarcoma survival was 1 year, which had not changed in 20 years. Fortunately, I had significant editing to do. There are new treatment modalities that are extending survival times and increasing the quality of life for dogs that cannot have surgery.

Osteosarcoma (OSA) is the most common primary bone tumor of dogs, with 85% of bone malignancies being attributed to this tumor. It is usually a cancer of large breed dogs with only 5% of OSA's occurring in dogs less than 15 kgs. Interestingly, if dogs less than 15 kgs have an OSA it is usually (59%) in the axial skeleton as opposed to large breeds who primarily have OSA in the appendicular skeleton. Increasing weight and height appear to be the most predictive factors for OSA in a dog. The breeds at most risk include Saint Bernards, Great Danes, Dobermans, Goldens and rescue Greyhounds. The classic "away from the elbow, towards the knee" is true for the elbow, however in the hindlimbs tumors are evenly distributed between the distal femur, distal tibia, and proximal tibia. Extraskelatal sites are rare and usually a grave prognosis. The primary rule outs for other primary bone tumors include lymphoma, fibrosarcoma, histiocytic sarcoma, hemangiosarcoma, multiple myeloma and chondrosarcoma.

Osteosarcoma has very aggressive local effects with the tumor causing bone lysis, bone proliferation, soft tissue swelling and eventual pathologic fractures. OSA rarely crosses a joint, if it does then histiocytic sarcoma, chondrosarcoma and synovial cell sarcoma are the differentials. Distant metastasis is common and arises early in the course of the disease, although usually not seen on screening diagnostics.

DIAGNOSTIC TECHNIQUES

Initial evaluation of the primary site includes interpretation of good-quality radiographs taken in lateral and craniocaudal projections. An OSA usually occurs in the metaphysis with tumors in the diaphysis classically being metastasis from another tumor. Features of OSA include cortical lysis, soft tissue swelling, new bone formation, loss of fine trabecular pattern in the metaphysis, a vague transition zone between at the periphery of the medullary extent of the lesion and the classic "Codman's Triangle". Codman's triangle is the tumor invading the cortex, lifting up the periosteum as new bone is being laid down, providing a triangular lesion on radiographs.

Based on signalment, history, physical exam and radiographs, a presumptive diagnosis of OSA can be made. If a dog has a suspicious travel history, osteomyelitis cannot be ruled out. A biopsy and culture is needed if this is the case. At this point a three view metastatic check may be warranted as the prognosis is guarded if the dog has pulmonary metastasis on presentation and the owner may not want to pursue further diagnostics. It should be noted that there are systemic therapies that can treat dogs with distant metastasis which will be discussed in treatment.

Arriving at a diagnosis can be achieved by a closed tissue biopsy, open tissue biopsy or a fine needle aspirate. In surgical oncology a biopsy is performed to get normal as well as tumor tissue, however with OSA this is an instance where the biopsy should be performed in the middle of the tumor as there is proliferative bone at the edges. All three techniques (open/closed biopsy, fine needle aspirate) have high sensitivity however the best technique is dependent on the lesion. A fine needle aspirate can be performed on a distal limb with a large lesion, however an open biopsy under fluoroscopy/mri/ct may have to be performed on a subtle lesion in the vertebrae, pelvis etc. However if a client has financial concerns and the lesion is amenable to fine needle aspiration, the sensitivity is 100% and specificity is 100% with alp staining. There are also urine telopeptides that correlate with increased bone lysis, however it cannot distinguish between osteoarthritic bone lysis vs. neoplastic bone lysis.

STAGING

As mentioned previously, three view thoracic radiographs or a thoracic CT should be performed. As 4-5% of dogs have bone metastasis on presentation a full staging protocol would include scintigraphy, whole body ct or survey radiographs. This can be both arduous and expensive however and usually is not performed. A minimum database of a cbc/chemistry should be performed as often alp is an indicator of significant bone lysis and a worse prognosis. Also lymph nodes should be palpated that drain the mass, and aspirated if palpated as lymph node metastasis carries a poor prognosis.

PROGNOSTIC FACTORS

There are several prognostic factors for osteosarcoma and they should be taken into account before treatment options are discussed. The most telling prognostic factor is local or distant metastasis. In a recent paper lymph node metastasis at presentation occurs 4% of the time but even with amputation and chemotherapy the median survival time is 48 days. With distant metastasis (lung metastasis) the survival time was days to weeks, however the most recent study on Palladia shows extended survivals with lung metastasis. Interestingly dogs that have metastasis to bones and not to the lungs appear to have a longer survival time, the issue is to then control pain which will be discussed later. Other prognostic factors include grade, site (proximal humerus the worst for appendiculars and mandible/digit better), increased alk phos, the length of time between diagnosis and treatment, weight, age and expression of several molecular markers (PTEN – a tumor suppressor gene, COX II – an enzyme in the arachidonic acid pathway, EZRIN – scaffolding in metastasis, SIS – an oncogene and VEGF – a growth factor expressed in angiogenesis).

TREATMENT OPTIONS

In all cancer consultations/treatments it is important to discuss the primary tumor (treatment, chance of recurrence) and the propensity for the primary tumor to spread. With OSA initially the concern is pain management because of the aggressiveness of the tumor, however every client should be told that with aggressive local therapy (amputation, radiation, bisphosphonates) there is still the issue of metastasis. For local treatment there are the following options:

Amputation – the median survival time with amputation alone is 5 months, however if the dog is orthopedically sound this is the most economical, effective treatment for the local disease

Limb sparing surgery – this is mostly performed on distal radial lesions. The median survival time is the same as an amputation, however has a high infection rate, failure rate and is significantly more expensive and involves multiple rechecks.

Cyberknife/Stereotactic surgery – this is one-two doses of high energy radiation to the lesion. The median survival time is again, the same as amputation, however is expensive, has a high pathologic fracture rate.

Palliative radiation – this is 3-4 dose of radiation that alleviates pain, has a 50-94% response rate with onset of relief at 11-14 days. The median duration is 73-130 days, with median survival times of 122-233 days

Bisphosphonate therapy – this is a new technique for controlling bone pain and tumor lysis. This is given as an iv diuresis and its mechanism of action is to prevent osteoclast (the bone macrophage) activity and induce osteoclast apoptosis (programmed cell death). With a combination of palliative radiation and Zometa (zoledronate) the investigators from Illinois are reporting survivals of 13 months.

Medical management – this includes NSAIDS and pain medications such as tramadol. The median survival time is 107 days from initial diagnosis.

Once the primary tumor is controlled, chemotherapy is recommended as it doubles and even triples the survival time. The chemotherapy protocols contain platinum drugs (Cisplatin, Carboplatin) or anthracyclines (Adriamycin). There are several protocols however the median survival time remains one year, with 20% of dogs living two years. However with the advent of metronomic/immunotherapy, bisphosphonates and targeted therapies (Palladia/Kinavet) typical survivals are extended past the 1 year “ceiling” and it is typical to see most dogs living multiple years.

If surgery is not an option we treat with a combination of bisphosphonates, radiation, NSAIDS and Tramadol, with survival often being over a year. If treatment for OSA is pursued we tailor the protocol to the health of the pet, as well as financial and time concerns of the owners. It is important to realize that because there are so many valid treatment options for all stages of OSA that owners are given the information needed to make an informed decision.

Bisphosphonates

Bisphosphonates are a group of drugs that help decrease bone pain in primary or metastatic bone diseases, lower calcium levels, and may help delay the progression of disease. They work through several mechanisms, including inhibiting bone resorption, impeding osteoclast (cells that break down bone) activity, inducing apoptosis (programmed cell death) in osteoclasts (cells of malignancy in OSA), and also exert anti-angiogenic effects (inhibiting blood vessel formation that helps tumors grow and spread). The most common bisphosphonates used are pamidronate and zoledronate. They can be used alone for palliation, in combination with radiation, chemotherapy or definitive therapy for OSA.

Radiographs lesions seen in OSA. 1.) solitary lesion in metaphysis 2.) ill defined zone of transition between lesion and adjacent bone 3.) subcutaneous reaction/swelling 4.) cortical destruction 5.) new bone proliferation 6.) periosteal reaction – Codman’s triangle: elevation of peristeam away from the cortex



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PVSES was founded to provide high quality, specialized medical care to companion animal patients. Our practice is dedicated to serving the veterinary community as a partner in total patient

care. We offer comprehensive specialized services including endoscopy, Doppler ultrasound, surgery, 24-hour ICU care, and emergency and critical care. Our

staff is committed to providing compassionate and thorough medical care that meets the needs of the patient, client, and referring veterinarian.

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