CLINICAL SIGNS ASSOCIATED WITH BONE AND JOINT TUMORS

Appendicular tumors most commonly are associated with lameness. It usually is chronic and progressive, but occasionally dogs can present acutely with severe lameness associated with pathologic fracture. A firm to hard swelling might or might not be palpable, but pain usually is elicited on palpation of the affected site of the bone. Most dogs are otherwise clinically healthy (BAR, good energy level, good appetite, etc.)

Axial tumors can present with a variety of signs depending on the affected site. Pain is not always as obvious because these tumors do not involve weight-bearing bones, but usually these tumors still are painful on palpation. Dogs with vertebral tumors can present with pain, weakness, ataxia/proprrioceptive deficits, paresis/paralysis. Oral tumors can present with a visible and/or palpable mass, halitosis, dysphagia, anorexia, weight loss, bloody discharge from the mouth, pain upon opening the mouth, and/or exophthalmos. Nasal tumors commonly are associated with unilateral or bilateral epistaxis or bloody/mucopurulent nasal discharge, sneezing, stertorous breathing, facial deformity, and/or exophthalmos. Rib tumors commonly are associated with a palpable mass. Very advanced tumors can cause respiratory distress/dyspnea. Thoracic limb lameness also can be seen secondary to mechanical obstruction and/or brachial plexus involvement.

Polyostotic lesions (lesions involving multiple bones) can be associated with a variety of signs depending on the sites affected. Some dogs will present with generalized pain that cannot be localized on physical examination. However, if one or a few lesions are significantly more painful than the others, the dog might present with signs referable to only a small subset of the total number of lesions present.

Many of the tumors that affect bone can metastasize to a wide variety of locations outside of the skeletal system. Clinical signs associated with disseminated disease often are vague and nonspecific: lethargy, anorexia, etc. Dogs with pulmonary metastasis might exhibit a cough. Overt respiratory distress is less common, and typically only associated with advanced end-stage disease. Hypertrophic osteopathy and secondary lameness can be seen in dogs with pulmonary metastasis. A variety of other clinical signs can be seen depending on the site(s) of metastasis.

RADIOGRAPHIC FEATURES OF AGGRESSIVE BONE LESIONS

When assessing a bone lesion radiographically, one of the first decisions is to determine whether the lesion is aggressive or nonaggressive. A bone lesion is considered to be aggressive if it has any of the following Roentgen signs:

- Moth-eaten or permeative bony lysis
- Long, ill-defined margin between normal and abnormal bone
- Non-homogenous, interrupted periosteal bone formation
- Partial or complete lysis of bony cortex (long bones)
- Rapid progression of radiographic signs over time
There are only two broad differentials for aggressive bone lesions: cancer and infection. Cancer can be subdivided into primary bone tumors, soft tissue tumors that secondarily invade into bones, tumors that metastasize to bones, and occasionally hematopoietic tumors. Osteomyelitis can be subdivided into bacterial and fungal infections. The Roentgen signs used to define aggressive bone lesions cannot be used to reliably rank these differentials. That is, different diseases can have similar radiographic appearances. Lesion location, patient signalment, history, and clinical signs are all very valuable when narrowing and prioritizing your differential diagnoses.

DIFFERENTIAL DIAGNOSES FOR AGGRESSIVE BONE LESIONS

Primary bone tumors

Osteosarcoma (OSA) accounts for 85% of all primary bone tumors.

- Body size (weight, or more specifically height) is the strongest predictive factor. Compared to dogs weighing < 10 kg, dogs weighing > 30 kg are 60 times more likely to develop OSA, and dogs weighing 20-35 kg are 8 times more likely.
  - Specific breeds considered to be at increased risk include the Greyhound, Great Dane, Irish Wolfhound, Irish Setter, Doberman Pinscher, Rottweiler, German Shepherd, Golden Retriever, and Saint Bernard, Scottish Deerhound, and Borzoi.
- Median age at diagnosis is 7-10 years, but dogs of any age can be affected (reported range, 6 months to > 14 years). There is no strong gender predilection.
- Common tumor locations
  - 75% of OSAs arise in the appendicular skeleton, most commonly in the metaphyseal region of the long bones. The most commonly affected sites are the distal radius, proximal humerus (“away from the elbow”), distal femur, proximal tibia, and distal tibia (“towards the knee, sort of”).
  - 25% of OSAs arise in the axial skeleton, including ribs, mandible, vertebrae, skull, and pelvis.

Chondrosarcoma (CSA) accounts for 10% of all primary bone tumors.

- There are no strong breed or gender predilections. Median age is 8-9 years, but dogs of any age can be affected.
- Common tumor locations
  - Nasal cavity (30% of all CSAs),
  - Ribs (20%)
  - Appendicular skeleton (20%). When chondrosarcoma arises in the appendicular skeleton, it is often but not always in one of the sites where OSA classically occurs.

Fibrosarcoma (FSA) and Hemangiosarcoma (HSA)

- Both fibrosarcoma and hemangiosarcoma account for < 5% of all primary bone tumors.
- Both of these tumors arise more commonly in locations other than bone (FSA arises most commonly in subcutaneous tissues. HSA arises most commonly in the spleen, heart, and skin.). It is relatively rare for these tumors to arise in bone.
- There are no strong breed, age, or gender predilections.
- There are no strong site predilections.
Tumors that secondarily invade bone by direct extension from adjacent soft tissues

Joint tumors
Primary bone tumors rarely cross joints. A primary bone tumor should be suspected whenever aggressive bone changes are seen in the bones on both sides of the joint. The involvement of the affected bones might be asymmetric. Also, there usually is a large soft tissue component to the mass effect that can be seen radiographically.

Synovial cell sarcoma
- These tumors arise from type B synoviocytes. (Type B synoviocytes normally are responsible for synovial fluid production.)
- Large-breed dogs are affected most commonly, including Golden Retrievers and Flat-Coated Retrievers. Most are middle-aged at the time of diagnosis. There is no gender predilection.
- Synovial cell sarcomas can arise from any joint, but the stifle, tarsus, elbow, and shoulder are affected most commonly.

Histiocytic sarcoma
- These tumors arise from subsynovial dendritic antigen-presenting cells.
- Rottweilers, Golden Retrievers, Flat-Coated Retrievers, and Bernese Mountain Dogs are predisposed. Most are middle-aged or older at the time of diagnosis. There is no strong gender predilection.
- The stifle and elbow are affected most commonly, but tumors can arise from any joint.
- Tumors can be solitary, but some dogs present with disseminated disease involving lymph nodes, liver, spleen, lungs, and bone marrow.

Oral cavity
- Squamous cell carcinoma, melanoma, fibrosarcoma, ameloblastoma (acanthomatous eupils)
- Other oral tumors are seen, but they rarely as associated with any bony changes.

Nasal cavity
- Nasal adenocarcinoma, squamous cell carcinoma, undifferentiated carcinoma.
- CSA and OSA are also seen in the nasal cavity, but they are considered primary bone tumors arising from the nasal turbinates (see above).

Digits
- Squamous cell carcinoma, melanoma.
- Other digital tumors are seen, but they rarely are associated with any bony changes.

Tumors that metastasize to bone (distant metastasis; not direct local extension)
Metastatic lesions most commonly involve the vertebrae, ribs, humerus, and femur – areas where there is active hematopoiesis and a subsequent relative increase in vascular supply. Multiple bones usually are affected (polyostotic lesion), but it is possible for just one site to be affected. Often there is concurrent spread to other organs (lymph nodes, lungs, etc.) Carcinomas metastasize to bone more frequently than sarcomas.
- The carcinomas that metastasize to bone most commonly are prostatic, mammary, and transitional cell (urinary bladder) carcinomas.
In cats, bronchoalveolar carcinoma can metastasize specifically to the digits. This has not been reported in dogs.

There is no such thing as a primary bone carcinoma. However, sometimes only the bony metastases are identified, and the primary tumor cannot be identified even on post-mortem examination (metastatic carcinoma of unknown origin).

The sarcomas that metastasize to bone most commonly are osteosarcoma and hemangiosarcoma.

**Hematopoietic tumors**

*Solitary plasma cell tumor (myeloma), multiple myeloma, and rarely lymphoma* are associated with bony lesions

- Lesions are seen most commonly in bones where active hematopoiesis occurs throughout life: vertebrae, ribs, pelvis, proximal humerus and femur, and skull.
- Radiographically, the lesions usually are purely osteolytic, often being described as areas where the bone has been “punched-out.” Diffuse osteoporosis occasionally is seen as well.

**Osteomyelitis**

**Bacterial osteomyelitis**

- In dogs, the majority of osteomyelitis cases are bacterial in origin.
- Direct inoculation is the most common mechanism, and usually there are other complicating factors such as tissue ischemia, bone necrosis and sequestration, fracture instability, foreign material implantation, and/or local alteration of immune response or tissue metabolism.
- Spread of infection via the bloodstream from a distant site is rare in dogs and cats. When it does occur, immature animals are usually affected.

**Fungal osteomyelitis**

- Fungal organisms typically enter through the respiratory tract and then disseminate via the blood and/or lymphatics. Most patients are systemically ill and have clinical signs referable to diffuse organ involvement.
- Multiple bone lesions usually are identified.
- In the United States, the most common isolates are Blastomyces, Coccidioides, Histoplasma, and Cryptococcus. Less commonly, Aspergillus and Phialoconidium have been reported.

**DIAGNOSTIC EVALUATION OF AGGRESSIVE BONE LESIONS**

If pursuing definitive treatment, it is essential to obtain a definitive diagnosis based on histopathology, as treatment recommendations and prognoses differ widely for the differentials listed above. But there is some flexibility as to *when* the histopathologic diagnosis needs to be obtained. If in addition to signalment, history, physical examination, and radiographic findings all strongly support a diagnosis of a primary bone tumor, a pre-surgical biopsy should be offered to the client, but it is acceptable to proceed with definitive surgery (i.e. aggressive surgery, including amputation) before reaching a definitive diagnosis. If there is any suspicion that the lesion might be something other than a primary bone tumor, then a pre-surgical incisional biopsy is recommended since aggressive surgery/amputation is not indicated for all of the other differentials.
Even if cytology or incisional biopsy is performed prior to definitive surgery and a tentative diagnosis has been reached, when the tumor is removed in its entirety it still must be submitted for histopathologic evaluation. Cytology samples and small biopsy samples occasionally can be misinterpreted, and it is crucial to submit the entire sample for thorough evaluation to confirm any provisional diagnosis.

**Cytology**

Fine needle aspiration can be performed if the lesion is somewhat lytic and there is thinning or destruction of the cortex. (OSA typically arises from the medullary cavity.) If needed, ultrasound guidance can be used to identify areas of cortical lysis. An evaluable sample can be collected in up to 85-90% of dogs. In the remaining 10-15% samples are not evaluable because of low cellularity. Using routine stains alone, cytology is helpful in about 50% of cases. Specifically for dogs with OSA, cytology yields a definitive diagnosis in 20% of cases and a more general diagnosis of sarcoma is made in an additional 30% of cases. OSA cells will stain positive for alkaline phosphatase (ALKP) on cytochemistry. When ALKP cytochemistry is used in addition to routine stains, sensitivity is > 95% and specificity is 90%. Both osteosarcoma cells and normal osteocytes will stain positive for ALKP. Therefore, cytochemistry does not help distinguish normal bone cells from cancerous ones. All it can do is help distinguish OSA from some other type of sarcoma.

**Biopsy**

A bone biopsy can be performed using a Jamshidi bone biopsy needle. Use radiographs to select biopsy site. Unlike most other tissues, when biopsying bone the sample should be collected from the center of the lesion. This is because the growth of a tumor stimulates osteoclastic and osteoblastic changes in the adjacent bone, resulting in the formation of reactive bone. Collecting the biopsy from the center of the lesion minimizes the chances of sampling only reactive bone. *If only reactive bone is identified on a biopsy sample, then the biopsy should be interpreted as inconclusive. The underlying disease process cannot be determined, and neoplasia cannot be ruled out.*

In a study comparing results of Jamshidi biopsies to those obtained from specimens obtained by surgical excision or necropsy, the ability to distinguish tumor versus nontumor was around 90%. Accuracy in determining the specific tumor type was around 80%.

**CLINICAL STAGING FOR DOGS WITH BONE TUMORS**

The goals of clinical staging are to reach a definitive tumor diagnosis, determine the extent of the cancer (local extend and any possible metastasis), and assess overall patient health. The results of these tests are used to help make treatment recommendations and provide prognostic information.

**Required staging diagnostics for all patients with aggressive bone lesions**

- Complete history and physical examination
- Biopsy/histopathology for definitive diagnosis (see above section on tissue biopsy)
- CBC, chemistry panel, urinalysis
  - General health screen
  - For appendicular OSA, elevated serum ALKP is associated with a poorer prognosis.
Imaging of the primary tumor
- For appendicular tumors, radiography usually is adequate (see above section on radiography)
- For axial tumors, CT scan is preferable for planning surgery and/or radiation therapy.
- Three-view thoracic radiographs and/or thoracic CT
  - The lungs are the most common site for metastasis for primary bone tumors.
  - CT is more sensitive than radiography for detecting pulmonary metastasis. The size threshold to reliably detect a pulmonary nodule on CT images is 1 mm, compared to 7-9 mm on radiographs.
- Regional lymph node evaluation
  - Regional lymph nodes should always be palpated, and any enlarged lymph nodes should be evaluated with cytology or histopathology.
  - The rate of metastasis to regional lymph nodes depends on the tumor type.
    - OSA rarely metastasizes to regional lymph nodes (< 5%), but prognosis is very guarded when it does occur.

Additional diagnostics to consider
- Bone scintigraphy
  - The patient is given an intravenous injection of a bone-seeking radioisotope (usually technetium 99m conjugated to methylene diphosphonate [MDP] or ethylene diamine tetramethylene phosphonate [EDTMP]). The radioisotope localizes to areas of increased bone turnover and blood flow, and then is imaged using a gamma camera.
  - Scintigraphy is much more sensitive than radiographs for identifying bone neoplasia, although false positives can occur.
  - Scintigraphy is indicated in patients where bone metastasis is suspected or confirmed because it is a simple way to evaluate the entire skeleton and identify any additional sites of metastasis with high sensitivity.
- Abdominal ultrasonography
  - Imaging of the abdomen is indicated if the patient has a form of cancer that frequently metastasizes there, or if clinical signs/physical exam findings indicate possible intra-abdominal pathology.
    - Primary bone tumors rarely metastasize to abdominal organs, but they can occasionally. Abdominal ultrasonography is not routinely indicated, but might be indicated based on clinical signs, physical examination findings, and/or baseline blood work results.
    - Dogs with bone hemangiosarcoma can have concurrent visceral involvement (usually in the spleen).

DEFINITIVE TREATMENT: APPENDICULAR OSTEOSARCOMA
For dogs with no evidence of gross metastatic disease, treatment must address both the primary tumor and the almost-certain microscopic metastatic disease. Treatment options for the primary tumor include amputation, limb-sparing surgeries, and stereotactic radiation therapy. Adjuvant chemotherapy is indicated for the microscopic metastatic disease.

Amputation alone is a reasonable alternative. Removing the primary tumor is the most effective way to eliminate the pain associated with the primary tumor. Yes, survival times are much shorter when adjuvant chemotherapy is omitted, but quality of life during that time
typically is very good because it is pain free. In contrast, chemotherapy alone is not an effective treatment option for the primary treatment option and therefore should not be used as a sole treatment modality.

**Amputation**

Most dogs are excellent candidates for amputation. Obesity, neurologic disease, and/or concurrent orthopedic disease such as osteoarthritis must be severe before amputation is contraindicated. *If the dog is non-weight-bearing lame, it is demonstrating its ability to function post-amputation.* Complete forequarter amputation is recommended for tumors involving the thoracic limb. Hip disarticulation is recommended for most hind limb tumors. The only exception is proximal femoral tumors – hip disarticulation is more appropriate for these tumors.

For dogs treated with amputation alone, median survival is around 4-5 months. The 1-year survival rate is 10%, and the 2-year survival rate is 2%. In the largest study of dogs with appendicular osteosarcoma treated with amputation alone (162 dogs), the causes of death were pulmonary metastasis (70%), osseous metastasis (6%), concurrent pulmonary and osseous metastasis (5%), metastasis to other sites (2%), local recurrence at amputation site (2%), non-tumor related causes (13%).

**Limb-sparing surgeries**

Limb-sparing surgeries (also called limb-salvage surgeries) can be considered if a dog is not a candidate for amputation or if an owner refuses to consider amputation. A variety of techniques exist. In general, they all consist of removing the diseased portion of the bone, and then reconstructing the weight-bearing axis of the limb. For tumors involving the distal radius, the most common technique involves marginal resection of the tumorous bone and replacing it with either a fresh-frozen cortical allograft (i.e., a piece of sterilized bone from a donor cadaver) or a metallic prosthetic. Everything is then secured using a bone plate that is anchored in the normal proximal radius, the implant, and the metacarpals (arthrodesing the carpus). For distal ulnar tumors, a functional outcome can be attained with just a segmental ulnectomy. No implant is required, since the radius normally provides most of the weight-bearing support. There also is a case report of a proximal femoral OSA that was treated with marginal resection of the tumor and placement of a cortical allograft and customized hip-replacement prosthesis.

To be a candidate for a limb-sparing surgery, a dog must meet *all* of the following requirements:

- The primary tumor must be located in the distal radius, distal ulna, or proximal femur. OSA usually arises in the metaphysis, and the adjacent joint cannot be preserved when the tumor is removed. Excellent function is retained when the carpus is arthrodesed, but not the shoulder, stifle, or tarsus. As mentioned above, there is a case report of a combination limb-sparing and hip replacement surgery, but this required a customized prosthesis.
- The primary tumor should involve < 50% of the length of the affected bone. There needs to be enough normal bone left behind to attach the bone plate that anchors the allograft/implant.
- There should be minimal extension into the surrounding soft tissues. This reduces the risk of local recurrence in the surrounding soft tissues.
- There should not be any evidence of pathologic fracture, because this can increase the risk of seeding tumor cells into the surrounding soft tissues.
- There must not be any gross metastatic disease.
The post-operative complication rate associated with limb-sparing surgeries is much higher than that associated with amputation. Infection rates are > 40%. They usually can be controlled with long-term (sometimes life-long) antibiotic therapy. In severe cases implant removal or amputation is needed. Other complications include local recurrence (< 10%) and implant failure (< 10%), although these can be minimized through careful patient selection. Long-term prognosis is comparable to that seen with amputation.

**Stereotactic radiotherapy**
Standard definitive radiation therapy protocols are not very effective at controlling the primary tumor. Stereotactic radiotherapy is a specialized form of radiation therapy that uses extremely accurate image-guided tumor targeting and patient positioning. A higher biologically effective radiation dose can be delivered to the tumor in fewer fractions (usually 1 to 3) while sparing the surrounding normal tissues. In preliminary studies, survival times in dogs treated with stereotactic radiotherapy are comparable to those seen with amputation. However, pathologic fracture can occur in lesions with extensive bony lysis.

(As a terminology note, stereotactic radiotherapy is also called stereotactic radiosurgery, although it does not involve any surgery. Cyberknife radiotherapy is one type of stereotactic radiotherapy.)

**Adjuvant chemotherapy**
When systemic chemotherapy is administered after the primary tumor has been surgically removed, median disease-free interval and survival time is extended. However, cure rate are not improved and the vast majority of dogs still eventually succumb to metastatic disease. The chemotherapy drugs used most commonly are cisplatin, carboplatin, and doxorubicin. There is no uniformly accepted adjuvant chemotherapy protocol. These drugs have been used by themselves or in combination with one another. Protocol selection should be based on drug side effects, cost, and veterinarian comfort level with each of these drugs. I typically recommend using a single-agent carboplatin protocol.

**Carboplatin**
- 300 mg/m² IV q3 weeks for a total of 4-6 treatments
- Median survival is 10-12 months, 1-year survival rate is 40-50%, 2-year survival rate is 15-20%.
- While closely related to cisplatin, carboplatin is not nephrotoxic (saline diuresis not needed) and not as likely to cause severe GI signs. It is more myelosuppressive than cisplatin.

**Cisplatin**
- 70 mg/m² IV q3 weeks for a total of 4 treatments
- Survival times comparable to those seen with carboplatin
- Nephrotoxic. Contra-indicated in dogs with renal disease or heart disease (aggressive fluid diuresis needed to protect the kidneys). Typically causes moderate to severe GI signs.
- Cisplatin historically was the treatment of choice for canine OSA. However, carboplatin typically is used today because it is equally effective, less toxic, and relatively comparable in price now that generic preparations are available.
Doxorubicin

- 30 mg/m² IV q2 weeks for a total of 5 treatments.
- Median survival 8 months, 1 year survival rate is 35%, 2 year survival rate is 17%.
- Contraindicated in dogs with heart disease. Can cause mild to moderate GI signs and myelosuppression.

Combining drugs with different mechanisms is an attractive idea because it hopefully reduces the chances of the cancer cells becoming resistant to therapy. In practice, though, combination protocols to not offer any advantage over single-agent protocols. Cisplatin/doxorubicin and carboplatin/doxorubicin protocols have been evaluated. However, because of overlapping toxicities (cisplatin and doxorubicin both cause GI signs; carboplatin and doxorubicin both are myelosuppressive) when these drug combinations are used the individual drugs must be given on an alternating basis or concurrently at significantly reduced dosages. As a result, there is no net increase in anti-tumor benefit. As a result, combination protocols do not show any clinical benefit over single-agent protocols.

DEFINITIVE TREATMENT: AXIAL OSTEOSARCOMA

The biologic behavior of axial OSA usually is similarly aggressive to that of appendicular OSA (See below for important exceptions), and treatment guidelines therefore are similar. Aggressive surgery is recommended whenever possible. However, complete excision often is not possible because of proximity to vital adjacent structures (e.g. vertebral tumors and the spinal cord). As many of 50-80% of dogs with axial OSA succumb to local disease. Metastatic rates are lower for axial OSA, but only because a significant fraction of dogs die from their local disease before they have a chance to develop gross metastatic disease.

Given the limitations of surgery, radiation therapy plays a much more prominent role in the treatment of axial OSA. Historically, for tumors that could be debulked, a combination of surgery and adjuvant definitive radiation therapy were recommended. For tumors that were not amenable to surgery, palliative radiation therapy was recommended. However, if stereotactic radiotherapy is available, it should be considered in place of surgery and/or conventional radiation therapy. Based on information with appendicular OSA, stereotactic radiotherapy is as effective at controlling the local disease as complete surgical excision (amputation). However, it is important to remember that OSA tumor cells produce osteoid (immature bone matrix). This matrix persists even after all tumor cells are killed, and therefore the mass effect might not change significantly. This is important if the tumor is causing significant local effects (such as a vertebral OSA compressing the spinal cord). If clinical signs persist after radiation therapy, a debuking surgery should be considered.

Chemotherapy is recommended to help delay the progression of microscopic metastatic disease. The drugs used are the same as those for appendicular tumors. I still typically recommend single-agent carboplatin.

Mandibular osteosarcoma

The metastatic rate for mandibular OSA is only 28%. Treatment typically focuses on the primary tumor – surgery and/or radiation therapy. Adjuvant chemotherapy has not been shown to improve prognosis. When treated with surgery alone, the 1-year survival rate is 71%.
Nasal osteosarcoma

Nasal osteosarcoma has a much lower metastatic rate. In one pathology study, only 1 of 17 dogs (6%) had metastatic disease identified at necropsy (lungs). Radiation therapy, either definitive conventional radiation therapy or stereotactic radiotherapy, is recommended. Median survival with radiation therapy alone is 1-2 years.

TREATMENT: METASTATIC DISEASE

Aggressive therapy usually is ineffective for dogs once there is evidence of gross metastatic disease. Isolated responses to cisplatin and doxorubicin have been documented, but response rates are < 5% and when responses are identified they usually last for only a few weeks. When combinations of surgery, radiation, and chemotherapy are used to treat dogs with visible pulmonary and/or visceral metastasis, survival times typically are only 2-3 months. Prognosis is slightly better for dogs with only osseous metastasis; median survival is around 3-4 months. Survival times are comparable with palliative care alone. Consequently, once metastatic disease is identified, palliative care is usually recommended rather than aggressive therapy.

Palladia (toceranib phosphate) is a new tyrosine kinase inhibitor that targets a variety of receptor tyrosine kinases, including KIT, vascular endothelial growth factor receptor (VEGF-R) and platelet-derived growth factor receptor (PDGF-R). The latter two receptors play important roles in angiogenesis. Anecdotally, I have used this drug in a few dogs with pulmonary metastasis and in some saw stabilization of disease. This drug can be considered in dogs with gross metastatic disease that still are enjoying good quality of life. This underscores the importance of monitoring patients with periodic thoracic radiographs. I usually recommend that they be taken every 2-4 months.

TREATMENT: PALLIATIVE CARE

Palliative care is indicated when dogs are not candidates for definitive therapy due to the presence of metastatic disease or other concurrent diseases, when definitive therapy has failed, or when definitive therapy is declined by the family. Palliative care focuses primarily on controlling the pain associated with the primary tumor. It is important to remember that dogs express pain in more subtle ways than people. Lameness, appetite, and social behaviors usually are the best monitoring tools. A proactive, multi-modality approach typically works best. I usually start dogs on a combination of an NSAID, tramadol, and gabapentin right away. I then add in bisphosphonate therapy and/or palliative radiation therapy as needed.

When dogs are treated with palliative therapy alone, prognosis is similar to that seen with amputation alone if and only if pain can be adequately controlled. The treatments below are not as consistently effective at eradicating pain as amputation, and a significant percentage of dogs are euthanized much sooner.

Pain medications

- NSAIDs are one of the most effective drugs for orthopedic pain.
- Tramadol: 3-5 mg/kg PO q6-12 h
- Gabapentin: 10-15mg/kg PO q8-12 h
- Tylenol with Codeine #4 (60 mg codeine per tablet): 1-2 mg/kg of codeine PO q6-12 h
- Amantadine: 3-5 mg/kg PO q24 h
- Fentanyl: patches or topical Recuvyra
- Lidocaine (50 mgc/kg/min)/ketamine (10 mcg/kg/min) CRI: Typically administered for 12 to 24 hours

**Bisphosphonates**

Bisphosphonates are used to treat pain associated with bone destruction. They also strengthen the bone, which can help prevent pathologic fracture. Bisphosphonates inhibit bone resorption by inhibiting the formation of new osteoclasts, inhibiting the ability of mature osteoclasts to resorb bone, and inducing osteoclast apoptosis. There is some *in vitro* evidence that bisphosphonates might have some direct anti-tumor effects, although clinically this has not been appreciated consistently. The most commonly used bisphosphonate in veterinary oncology is pamidronate. Zolidronate is a newer generation bisphosphonate that is much more potent, but also considerably more expensive. Alendronate is an oral bisphosphonate that can be used, but the other intravenous drugs are preferable because oral bioavailability is quite variable.

**Pamidronate**

- 1-2 mg/kg IV in 250 mL saline over 2 hours q4 weeks
- 30% of dogs have clinical improvement in lameness. Median response duration was 7 months (range 4-12 months).
- All dogs have improved bone strength based on increased relative bone mineral density and decreased markers of bone turnover.
- When used in combination with palliative radiation therapy and chemotherapy, there was no improvement in long-term survival. This indicates little to no clinical anti-tumor benefit.

**Zolidronate (Zometa)**

- 0.1 mg/kg IV in 60 mL saline over 15 minutes
- Subjective pain improvement in about 75% of dogs with appendicular OSA
- In a preliminary study (abstract only), when zolidronate was combined with palliative radiation therapy, median progression free survival was 350 days. This is better than what is seen with amputation, indicating that perhaps this treatment combination might also have anti-tumor benefits that delay the progression of metastatic disease.

**Palliative radiation therapy**

Palliative radiation therapy consists of a hypofractionated protocol. One of the most commonly used protocols consists of 1 treatment per week for 4 consecutive weeks. Palliative radiation therapy does not significantly slow the progression of the primary tumor, but it helps relieve pain in 75-90% of dogs with appendicular OSA. It can take a few weeks to reach maximum response, so other more quickly acting treatments such as oral analgesics and bisphosphonates should be used while waiting for clinical response. Pain relief typically persists for 2-3 months. Palliative radiation therapy typically is not repeated, but this can be considered for dogs that have exceptional responses. As discussed with stereotactic radiosurgery, if the tumor is especially lytic, as the dogs becomes more comfortable and starts to bear more weight on the affective limb, there is a risk of pathologic fracture.