

Osteosarcoma Update

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Introduction

Appendicular osteosarcoma is the most common form of primary bone cancer in dogs. It primarily affects middle-aged to older dogs of large and giant breeds. It is important to note that the median age at presentation is 7 years, but there are two peaks in age at presentation. The large peak is in dogs 7-9 years of age, but there is also a small peak at 18-24 months of age. The presentation will vary with the progression of disease and the timing with which the owner elects to bring their dog for evaluation. The lameness can be mild to severe, acute to chronic. It is possible that mild cases that are early in their progression will respond to rest and NSAID therapy. If this treatment is elected in large breed dogs, it is important to recheck the patient after 5-7 days to evaluate whether or not the pain or lameness persists and further work up should be recommended in these cases. It is also possible that this disease will present as a pathological fracture. This is generally associated with low impact trauma such as playing in the park or jumping out of the car or off furniture.

Typically osteosarcoma is metaphyseal and endosteal in origin. The most common sites are the distal radius and proximal humerus, followed by the distal femur and proximal tibia. This has led to the adage, "away from the elbow, towards the knee". Although this holds fairly true in the forelimb, the tibia and femur can present in proximal or distal locations and it is important to remember that although these are the most common sites, other sites can be affected.

Diagnostic Work Up

The decision to biopsy a suspect primary aggressive bone lesion will depend on the clinician's preference and the characteristics of the patient and lesion. Some clinicians will biopsy every bone site and others will only biopsy if there is an atypical signalment, location or radiographic appearance in cases that are consistent with osteosarcoma. It is important to consider fungal osteomyelitis in endemic areas. Potential risks of bone biopsy include increased lameness after the procedure, pathological fracture, a non-diagnostic sample and increased complications in limb spare candidates. The risk of a non-diagnostic sample is decreased by taking the biopsy from the centre of the lesion. For distal radial lesions where limb spare may be an option, the biopsy must be taken from one small incision as the biopsy tract must be removed with resection of the distal radius. The risk of pathological fracture after treatment with stereotactic radiosurgery is also a concern for patients that may receive this treatment modality. Because of the risks, time and expense involved in bone biopsy, many clinicians opt out of this diagnostic test. A fine needle aspirate is an option with less risks and the benefit of a diagnosis of sarcoma or osteosarcoma in most cases. The diagnostic yield may be increased using ultrasound guidance. This technique will be painful and heavy sedation or general anesthesia is required. I use a large gauge needle (18-20G) to improve the diagnostic yield. ALP staining may help to differentiate an osteosarcoma from a sarcoma cytologically.

However, in most cases, the treatment of all primary sarcomas of bone will be similar.

Most cases (>90%) of canine osteosarcoma have micrometastasis at the time of presentation. Staging is done to determine if there is evidence of gross metastasis. Current recommendations for staging of osteosarcoma include evaluation of the lungs with three-view thoracic radiographs and a bone scan to assess for bone metastasis. The rate of finding gross lung metastasis is around 10%. This is slightly increased by thoracic CT and this is becoming a more common method of staging the lungs. Bone staging is more challenging at centres where scintigraphy is not readily available. Long bone survey radiography has been reported as a method of long bone staging, with up to 7.8% of dogs being positive for bone metastasis. However, in the author's experience, the rate of detecting bone metastasis with long bone survey radiography is much lower than this. Whole body CT scan is used at some centres for long bone staging. However, a recent study indicated that this method is an insensitive test for long bone staging and should be reserved for specific assessment of lesions that were previously detected on scintigraphy. Draining lymph nodes should be assessed with palpation, FNA if accessible and histopathology if the limb is amputated. The rate of metastasis to the lymph nodes is low, but carries a worse prognosis. Full blood work and urinalysis should be performed to ensure that the patient is overall healthy and can undergo treatment. The ALP has been shown to be a prognostic indicator in dogs and humans with osteosarcoma.

Treatment

The most common treatment of dogs with osteosarcoma is limb amputation. Most dogs tolerate this procedure extremely well and will adapt quickly to being on three legs. It is important that a full orthopedic examination is performed prior to amputation to assess for potential contraindications for limb amputation and to assess for pain at other bone sites that may be consistent with metastasis. Mild or moderate DJD in other joints is not considered a contraindication for amputation. Most dogs with osteosarcoma are not using the affected limb well and this will give the owner and attending clinician an idea of how well they will do on three legs.

For patients that will not tolerate amputation, limb salvage procedures are available at select centres. A surgical limb spare is most often performed for lesions of the distal radius and usually involves resection of the affected distal radius with an adequate margin and the use of a metal endoprosthesis spacer to fill the defect. The endoprosthesis is secured using a specialized bone plate that spans from proximal radius to metacarpals. Stereotactic radiotherapy (SRT) is an option for lesions at other sites. This involves the administration of a high dose of radiation to the bone tumor, with little to no radiation given to the surrounding normal structures. This is a relatively new procedure but it holds promise for treatment of osteosarcoma in dogs. It is important to remember that although it is rare, it is possible to perform a limb salvage procedure for primary bone tumors of the ulna by ulnectomy or partial ulnectomy or of the scapula by complete or partial scapulectomy. Other than cost,

the biggest downside to SRT is the high risk of pathological fracture, with rates of up to 60% reported.

After aggressive local therapy, systemic chemotherapy is recommended as adjuvant therapy for osteosarcoma. This has been shown to significantly increase survival time. Dogs that are treated with amputation alone will succumb to disease in 3-5 months, whereas dogs treated with amputation or limb spare and chemotherapy will live for 9-12 months. Palliative amputation may still be appropriate in cases where the owner is not willing to pursue chemotherapy because the quality of life will be much better with removal of the primary tumor.

Palliative therapy may also be elected in the form of palliative radiation therapy and analgesics. Of all of the palliative approaches, palliative radiation is thought to have the most significant impact on pain control. Analgesia provided should be a combination of NSAIDs, bisphosphonates, opioids and gabapentin. Chemotherapy may also help to treat pain and slow the progression of disease. These patients must be monitored carefully to assess their quality of life and euthanasia should be recommended in cases where the patient remains painful or becomes painful again. Many dogs with chronic pain will not cry out or change their behavior much and it is very important to educate owners that the best way to assess pain due to osteosarcoma is to evaluate limb use. Other factors that should be assessed include activity, appetite, willingness to participate in normal activities with the owners and ability to sleep soundly and dream.

References

- 1: Talbott JL, Boston SE, Milner RJ, Lejeune A, Souza CH, Kow K, Bacon NJ, Hernandez JA. Retrospective Evaluation of Whole Body Computed Tomography for Tumor Staging in Dogs with Primary Appendicular Osteosarcoma. *Vet Surg*. 2017 Jan;46(1):75-80. doi: 10.1111/vsu.12579. PubMed PMID: 27906470.
- 2: Pagano C, Boudreaux B, Shiomitsu K. SAFETY AND TOXICITY OF AN ACCELERATED COARSELY FRACTIONATED RADIATION PROTOCOL FOR TREATMENT OF APPENDICULAR OSTEOSARCOMA IN 14 DOGS: 10 GY \times 2 FRACTIONS. *Vet Radiol Ultrasound*. 2016 Sep;57(5):551-6. doi: 10.1111/vru.12389. PubMed PMID: 27374864.
- 3: Khanna C. The current state and a perspective towards the future of osteosarcoma in dogs. *Vet Comp Oncol*. 2016 Jun;14(2):e1-3. doi: 10.1111/vco.12237. PubMed PMID: 27140205.
- 4: Kubicek L, Vanderhart D, Wirth K, An Q, Chang M, Farese J, Bova F, Sudhyadhom A, Kow K, Bacon NJ, Milner R. ASSOCIATION BETWEEN COMPUTED TOMOGRAPHIC CHARACTERISTICS AND FRACTURES FOLLOWING STEREOTACTIC RADIOSURGERY IN DOGS WITH APPENDICULAR OSTEOSARCOMA. *Vet Radiol Ultrasound*. 2016 May;57(3):321-30. doi: 10.1111/vru.12351. PubMed PMID: 26916056.
- 5: Schmidt AF, Groenwold RH, Amsellem P, Bacon N, Klungel OH, Hoes AW, de Boer A, Kow K, Maritato K, Kirpensteijn J, Nielen M. Which dogs with appendicular osteosarcoma benefit most from chemotherapy after surgery? Results from an individual patient data meta-analysis. *Prev Vet Med*. 2016 Mar 1;125:116-25. doi: 10.1016/j.prevetmed.2015.10.016. PubMed PMID: 26796424.
- 6: Mitchell KE, Boston SE, Kung M, Dry S, Straw RC, Ehrhart NP, Ryan SD. Outcomes of Limb-Sparing Surgery Using Two Generations of Metal Endoprosthesis in 45 Dogs With Distal Radial Osteosarcoma. A Veterinary Society of Surgical Oncology Retrospective Study. *Vet Surg*. 2016 Jan;45(1):36-43. doi: 10.1111/vsu.12423. PubMed PMID: 26731595.
- 7: Selmic LE, Burton JH, Thamm DH, Withrow SJ, Lana SE. Comparison of carboplatin and doxorubicin-based chemotherapy protocols in 470 dogs after amputation for treatment of appendicular osteosarcoma. *J Vet Intern Med*. 2014 Mar-Apr;28(2):554-63. doi: 10.1111/jvim.12313. PubMed PMID: 24512451; PubMed Central PMCID: PMC4857984.
- 8: Schmidt AF, Nielen M, Klungel OH, Hoes AW, de Boer A, Groenwold RH, Kirpensteijn J; V.S.S.O. Investigators.. Prognostic factors of early metastasis and mortality in dogs with appendicular osteosarcoma after receiving surgery: an individual patient data meta-analysis. *Prev Vet Med*. 2013 Nov 1;112(3-4):414-22. doi: 10.1016/j.prevetmed.2013.08.011. PubMed PMID: 24054333.

9: Oblak ML, Boston SE, Woods JP, Nykamp S. Comparison of concurrent imaging modalities for staging of dogs with appendicular primary bone tumours. *Vet Comp Oncol.* 2015 Mar;13(1):28-39. doi: 10.1111/vco.12016. PubMed PMID: 23421618.

10: Ryseff JK, Bohn AA. Detection of alkaline phosphatase in canine cells previously stained with Wright-Giemsa and its utility in differentiating osteosarcoma from other mesenchymal tumors. *Vet Clin Pathol.* 2012 Sep;41(3):391-5. doi: 10.1111/j.1939-165X.2012.00445.x. PubMed PMID: 22676437.

11: Armbrust LJ, Biller DS, Bamford A, Chun R, Garrett LD, Sanderson MW. Comparison of three-view thoracic radiography and computed tomography for detection of pulmonary nodules in dogs with neoplasia. *J Am Vet Med Assoc.* 2012 May 1;240(9):1088-94. doi: 10.2460/javma.240.9.1088. PubMed PMID: 22515629.

12: Neihaus SA, Locke JE, Barger AM, Borst LB, Goring RL. A novel method of core aspirate cytology compared to fine-needle aspiration for diagnosing canine osteosarcoma. *J Am Anim Hosp Assoc.* 2011 Sep-Oct;47(5):317-23. doi: 10.5326/JAAHA-MS-5676. PubMed PMID: 21852507.

13: Eberle N, Fork M, von Babo V, Nolte I, Simon D. Comparison of examination of thoracic radiographs and thoracic computed tomography in dogs with appendicular osteosarcoma. *Vet Comp Oncol.* 2011 Jun;9(2):131-40. doi: 10.1111/j.1476-5829.2010.00241.x. PubMed PMID: 21569198.

14: McMahon M, Mathie T, Stingle N, Romansik E, Vail D, London C. Adjuvant carboplatin and gemcitabine combination chemotherapy postamputation in canine appendicular osteosarcoma. *J Vet Intern Med.* 2011 May-Jun;25(3):511-7. doi: 10.1111/j.1939-1676.2011.0697.x. PubMed PMID: 21488959; PubMed Central PMCID: PMC3807042.