

# *Multilobular Osteochondrosarcoma*

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## **INTRODUCTION**

Multilobular osteochondrosarcoma (MLO) has been known by many different names, including chondroma rodens, calcifying aponeurotic fibroma, cartilage analogue of fibromatosis, multilobular chondroma or osteoma, and most recently multilobular tumor of bone.<sup>4,8,11</sup> These were mostly used due to its histologic resemblance to human tumors.<sup>9</sup> Multilobular osteochondrosarcoma or multilobular tumor of bone is a primary tumor of bone that is found on the flat bones of the skull.<sup>3,4,9</sup> It is the most common tumor found on the skull of dogs.<sup>14</sup> Although not specific to the dog or skull, rare reports have been confirmed in the cat, horse, and ferret, and in the os penis of a dog.<sup>4,9,13</sup>

## **HISTORY AND PRESENTATION**

Typical presentation of a multilobular tumor of bone is seen in a middle aged to older, medium to large breed dog.<sup>3,4,9,10,11,12</sup> There is no sex predilection, and the patient will present with a firm, non-painful, fixed mass located on the skull.<sup>3,4,9,10,11,12</sup> Although, these masses are mostly found on the calvarium, they can also be found on the maxilla, mandible, orbit, tympanic bulla, or zygomatic bones.<sup>4</sup> Some MLO cases can present with more advanced signs due to the placement and extensiveness of the tumor.<sup>9</sup> The larger tumors may apply pressure on structures of the face such as the eyes, tympanic bulla, or mandible causing exophthalmos, dyspnea, and pain on opening of the mouth, respectively.<sup>9,12</sup> Neurological signs can be seen in patients that have large tumors located on the cranium that are compressing the brain.<sup>12</sup>

## **PATHOPHYSIOLOGY**

MLO is an uncommon tumor and the histogenesis and pathophysiology are not completely understood.<sup>4,8,11,12</sup> There are two main theories regarding the origin of MLO. The background for the first theory is that flat bones of the skull develop by intramembranous

ossification and the tumor's lobular appearance is from abnormal cellular activity of the periosteum from bones developed by this process.<sup>4,7</sup> The second theory is that MLO arises from cells that have a common embryonic lineage.<sup>4, 8,11,12</sup> The chondrocranium is made up of the bones that surround the brain and is also known as the neurocranium.<sup>2</sup> The viscerocranium is made up of the bones that make up the facial skeleton such as the maxilla, mandible, and zygomatic bones.<sup>2</sup> The chondrocranium and viscerocranium both originate from neural crest cells.<sup>8</sup>

### **DIFFERENTIAL DIAGNOSES**

MLO is the most common cause of masses on the skull of dogs, however there are other possibilities that should be examined.<sup>14</sup> The first of which are non-neoplastic, such as tooth root abscesses, foreign bodies, and/or orbital cellulitis.<sup>3,5</sup> These can cause swellings on the face, on the mandible or around the eye. These three options will more than likely respond to antibiotics and are usually painful on presentation.<sup>5</sup> Osteosarcoma and MLO are the two most common neoplastic causes of tumors located on the calvarium.<sup>3</sup> Sarcomas such as hemangiosarcoma, fibrosarcoma and chondrosarcoma are other differential diagnoses.<sup>3</sup> In addition to the sarcomas, mast cell tumors, adenomas and primary optic nerve neoplasia are differential diagnoses for tumors around the eye.<sup>3</sup> Soft tissue sarcomas are another rule out for tumors found anywhere on the skull.<sup>3</sup>

### **DIAGNOSTIC APPROACH/CONSIDERATIONS**

A minimum database consisting of complete blood count, blood chemistry panel, and urinalysis should be performed prior to any advanced diagnostic procedures. This will help rule out any underlying processes that may exist concurrently with the tumor.

Masses located on the skull of dogs can appear similar in clinical presentation; therefore it is essential that a histological definitive diagnosis, including tumor grade, be pursued via biopsy.<sup>3</sup> Three-view thoracic radiographs should be completed to identify pulmonary metastasis.<sup>3</sup> Computed Tomography (CT) is useful for surgical planning.<sup>3</sup> It can be used to determine the tumors involvement in surrounding tissue. The tumor has a multilobular, granular appearance with well-defined margins.<sup>12</sup> A magnetic resonance imaging (MRI) study can also be an option, however CT is often preferred due to being faster and less expensive.<sup>3</sup> MRI has been found to be more useful if there is suspected CNS or soft tissue involvement and to visualize the extent of skull tumors.<sup>3,12</sup>

As previously stated, a diagnosis of MLO is made upon histologic evaluation.<sup>3</sup> Histologic characterization of MLO is irregular lobules of cartilaginous tissue, osseous tissue or both.<sup>9</sup> These lobules are surrounded by thin fibrovascular septa and mesenchymal tissue.<sup>9,12</sup> The lobules consist of chondrocytes that may or may not be surrounded by chondroid matrix.<sup>9</sup> Some areas may have mesenchymal cells producing bony matrix undergoing ossification.<sup>9</sup> Mitotic figures may or may not be present.<sup>8,9</sup>

### **TREATMENT AND MANAGEMENT OPTIONS**

Surgical excision with complete margins are the treatment of choice for this tumor and can be curative in some cases.<sup>6,14</sup> Incomplete surgical margins have been shown to significantly decrease the time to local recurrence.<sup>4</sup> When performing surgeries to remove MLO such as craniectomy, mandibulectomy, orbitectomy, it is important to have clean surgical margins. An attempt to obtain one to two centimeter margins around the mass should be made when performing excision.<sup>3</sup>

Adjuvant therapies have been proposed, but not extensively studied. Chemotherapy is a common therapy with osteosarcoma, however with MLO it has not been shown to prevent local recurrence or metastasis.<sup>3</sup> In a retrospective study of 39 dogs, only 9 dogs received adjuvant therapy consisting of chemotherapy (biodegradable polymer containing cisplatin or intravenous cisplatin), radiation therapy (external beam or intraoperative radiation), or both chemotherapy and radiation.<sup>4</sup> Cases that received adjuvant therapy were those that were more advanced, meaning they could not be resected or clean margins were not obtained after histologic confirmation.<sup>4</sup> Six cases received local chemotherapy, one of which also received radiation therapy.<sup>4</sup> One case received radiation therapy only, and two cases received both intravenous chemotherapy and radiation therapy.<sup>4</sup> Of the cases that received only chemotherapy, three developed local recurrence and one developed local recurrence and metastasis.<sup>4</sup> Of the cases that received local chemotherapy and/or radiation therapy, both returned with metastasis and/or local recurrence.<sup>4</sup> The same can be said for those cases receiving intravenous chemotherapy and radiation, indicating a 100% local recurrence rate and a 50% metastatic rate.<sup>4</sup> No set standards or protocols were used to study the doses or style of the adjuvant therapy. Because of these limitations, it is difficult to say with certainty whether these ancillary treatment options would be beneficial to all patients diagnosed with MLO. Finally, pulmonary metastastectomy is another option for dogs with few to minimal pulmonary metastatic nodules.<sup>4</sup> Dogs that underwent this surgery had a significant increase in survival times.<sup>4</sup>

### **EXPECTED OUTCOME AND PROGNOSIS**

Tumor location, clean surgical margins, and histological grade of the tumor are the negative prognostic indicators associated with MLO.<sup>4,12</sup> The anatomical location of the tumor can determine the difficulty or lack thereof allowing for complete resection and clean surgical

margins. MLO located on the mandible had the highest median survival time compared to non-mandibular sites.<sup>4</sup> Mandibulectomy procedures are likely to remove the entire tumor therefore decreasing the chance of recurrence. An interesting observation is that the size of the tumor as a whole is not proven to have an effect on prognosis.<sup>4</sup> As stated previously, inadequate surgical margins can decrease the time to local recurrence.<sup>4</sup> In one retrospective study, 8 of 19 cases with complete margins had local recurrence versus 10 of 13 cases with incomplete margins.<sup>4</sup> The median time to local recurrence was also decreased with incomplete margins.<sup>4</sup> However, the number of surgical resections did not have an impact on local recurrence, metastasis, or survival time. The final negative prognostic indicator is histologic grading. Histologic grading for MLO is based on the six following criteria: borders (invading, pushing, or both), size of lobules, organization, mitotic figures, pleomorphism, and necrosis.<sup>4</sup> Each of these criteria are given a score, the number is then tallied and corresponds with a tumor grade. Tumor grade had a direct correlation with local recurrence and metastasis, the greater the tumor grade the more likely the probability of local recurrence and also metastasis.<sup>4</sup>

## **CONCLUSION**

In conclusion, MLO is a slow growing, slow to moderately metastatic neoplasm of the skull bones.<sup>4</sup> There are no known breed or sex predilections related to MLO.<sup>3,4,9,10,11,12</sup> This type of neoplasia mostly affects middle aged, medium to large breed dogs.<sup>3,4,9,10,11,12</sup> Location, tumor grade, and clean surgical margins are the most efficacious prognostic indicators.<sup>4,12</sup> More data is needed to determine the effectiveness of other treatments such as chemotherapy and radiation therapy.<sup>4,12</sup>

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