Radiodiagnosis Role in Differentiating between Benign and Malignant Bone Tumors

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Abstract
The evaluation of bone tumors can be a challenge to any practitioner. The goal is to discern the benign bone lesion from the malignant bone lesion in the office or hospital setting. When evaluating a patient with a bone lesion, it is important to take multiple factors into consideration. One usually can narrow the probability of a tumor being benign or malignant based on the patient's age, location of the lesion in the body, the lesion's location within the bone and radiographic findings. Due to the rarity of primary malignant bone neoplasms and the varied imaging presentation of focal bone lesions, radiologists outside oncology centers tend to have little experience in reporting this type of anomaly. Thus, imaging reports might be unclear and misleading, increasing the risk of misdiagnosis and suboptimal patient management. Bone tumors can be a challenge to even the most experienced radiologist or oncologist. The key to differentiating the benign from the aggressive and potentially malignant lesion is to understand the basic radiographic differences between the two. The podiatric physician should be able to narrow down the differential diagnosis based on the patient's clinical findings, age, the lesion's location in the bone and the radiographic appearance of the tumor.
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Introduction
The evaluation of bone tumors can be a challenge to any practitioner. The goal is to discern the benign bone lesion from the malignant bone lesion in the office or hospital setting. When evaluating a patient with a bone lesion, it is important to take multiple factors into consideration. One usually can narrow the probability of a tumor being benign or malignant based on the

patient's age, location of the lesion in the body, the lesion's location within the bone and radiographic findings.1

However, it is important to note that this is not always uniformly true. Aggressive lesions may tend to be malignant although certain benign tumors may also display similar characteristics.2 It is also equally important to try to determine whether a lesion is a "primary" tumor or a "secondary" bone tumor, which has metastasized from another region of the body. Characteristically, many malignant tumors have clinical symptoms of pain associated with the lesion but this also can be true of some benign tumors.

The most useful modality for evaluating a bone lesion is the plain film radiograph. The advantage of radiographs is that they can provide essential information and characteristics as to the bone tumor's size, location and aggressiveness when you are evaluating a primary lesion.1,3,4 Radiographic findings can certainly aid in the differential diagnosis and directing attention to the pattern of bone destruction and periosteal response is important.

After determining a suspected lesion is likely aggressive and possibly malignant, utilize other imaging modalities. Magnetic resonance imaging (MRI) is considered the "modality of choice" when the lesion in question is likely malignant.1 The advantage of MRI is the ability to evaluate bone marrow changes and the extent of a lesion. The disadvantage of MRI is that it may lack specificity due to many lesions having findings of a low T1 and high T2 signal, which can represent "edema, pus and tumor" infiltrate.1

Computed tomography (CT) scans can also be beneficial in observing bony changes that are more subtle than plain radiographs can represent. Computed tomography scans can also be useful in bone biopsies.1,5

Particularly when it comes to cases of metastatic lesions, bone scintigraphy is another imaging technique, which is very sensitive in detecting bone turnover with Tc-99m bisphosphonate.6 If any doubt remains, confirm the definitive diagnosis of a bone lesion via bone biopsy.

A Guide To Radiographic Presentations Of Aggressive And Benign Bone Lesions

The radiographic appearance of bone lesions and their pattern of bone destruction can yield clues to the aggressive versus benign state of a particular lesion. Periosteal reactions can be a guide to the aggressiveness of the lesion as well. However, benign and malignant bone lesions can have a "high degree of overlap" and aggressive lesions can have relatively "benign appearing periosteal reaction or none at all."1,7 This also holds true for patterns of bone destruction in relation to lesions that appear less aggressive.

There are three types of bone destructive patterns: geographic, moth-eaten and permeative.

Benign bone lesions typically display geographic bone destruction. This type of lesion usually is a slow growing tumor with well-defined margins. Lesions that demonstrate thicker sclerotic margins also tend to be less aggressive.2 Although this pattern is usually benign, be aware that this pattern can also be present with malignant diseases, osteomyelitis and metastatic pathology. Accordingly, this pattern does not always suggest a benign process.2

The moth-eaten pattern of bone destruction indicates a more aggressive lesion. There may typically be a longer zone of transition between normal and abnormal bone, which is indicative of a rapidly growing lesion. Malignancies and osteomyelitis can display this pattern.

Permeative bone destruction indicates a malignant process with poorly defined margins. These lesions are rapidly growing and poorly demarcated.

Periosteal responses can help aid in the assessment of bone lesions as to the relative aggressiveness of the lesion in question. Typically, periosteal buttressing and thickening of the periosteum are indicative of a slow growing lesion with the process of the tumor slowly "eroding" the cortices of bone with new periosteal bone formation.2

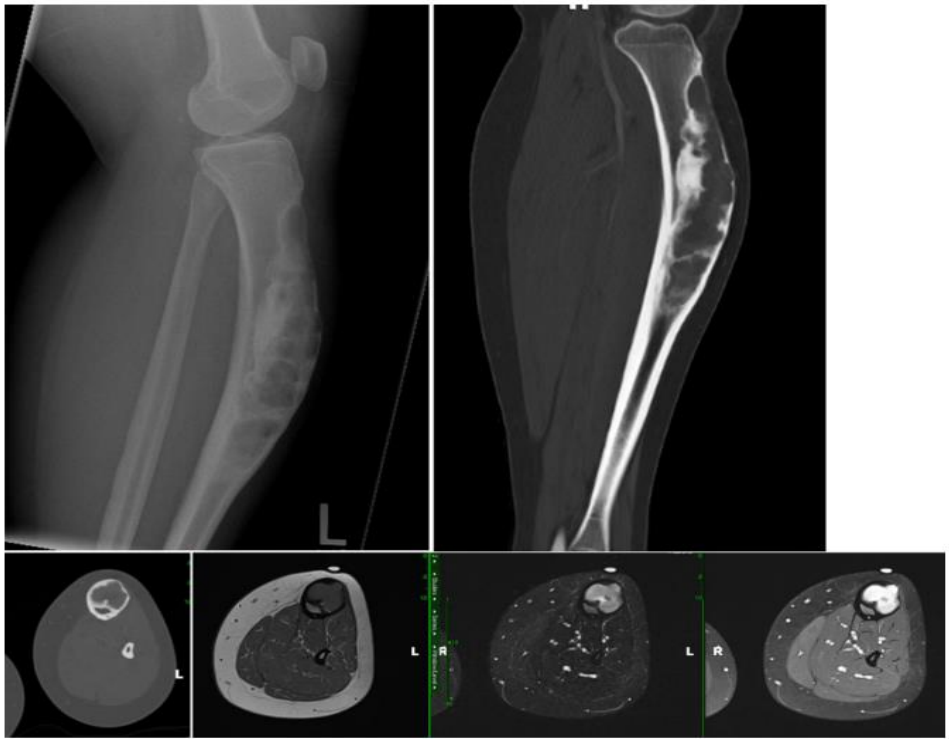

Figure 1: Benign bone lesion in a 15-year-old girl. (Top) Lateral radiograph and sagittal CT reconstruction of the left tibia demonstrate a well-defined, geographic, cortically based, diaphyseal mixed lytic and sclerotic lesion along the anterior tibia with marginal sclerosis and areas of dense osteoid mineralization. (Bottom) Axial CT, T1-weighted, STIR, and contrast-enhanced MRIs demonstrate a lytic lesion with fibrous matrix involving the anterior tibial cortex with circumferential sclerosis, which encroaches on but does not invade the medullary cavity. Biopsy-confirmed osteofibrous dysplasia

Other periosteal reactions are indicative of rapid and possibly aggressive tumor growth. Codman's triangle is a triangular elevation of the periosteum due to an aggressive lesion that is protruding through the bony cortex. Sunburst and hair-on-end periosteal formations also are associated with aggressive bone tumors and are radiating spicules of periosteal bone. The onion peel pattern of periosteal response is a pattern of multiple layers of new periosteal bone formation and associated with aggressive bone lesions.

The position of the tumor within bone can aid in the diagnosis of the tumor. It is important to obtain multiple plain film views to ascertain the position of the lesion in both the transverse and longitudinal planes.

Lesions in the transverse plain are identified as follows: central, eccentric, cortical and juxtacortical. For example, enchondromas are typically located in the central portion of the medullary canal and referred to as central lesions. Most bone tumors have a predilection for a position within bone in the transverse plane as well as the longitudinal plane. In long bones, these planes are the epiphysis, metaphysis and diaphysis. For example, osteosarcomas and chondrosarcomas tend to be metaphyseal lesions.

The amount of reactive bone marrow edema and peritumoral edema can give insight into the aggressiveness of a primary bone lesion. The advantage of MRI is the high sensitivity to fluids on both the T2 and short tau inversion recovery (STIR) images.1 Studies have found that in assessing a bone tumor, less bone marrow edema may correlate with an increased probability of a malignancy.1,8,9 Therefore, increased marrow edema around a small tumor more likely indicates a benign process.1 These findings are generally non-specific but may aid in the differentiation of a questionable bone tumor.

A Pertinent Overview Of Malignant Bone Tumors

When it comes to diagnosing most bone lesions, one must take many factors into consideration. Physicians usually cannot make an accurate diagnosis based on imaging findings alone. The clinical presentation, patient age, location and site of the bone lesion, and radiographic findings are crucial to accurate diagnosis.3,10

One study by Ma and colleagues found that MRI studies along with plain films and clinical findings yielded a 73 percent diagnostic accuracy rate of malignant and benign tumors in comparison to just 55 percent with MRI alone.1,11 The following is a representation of the clinical and radiographic findings to aid the podiatric practitioner in the differentiation of benign versus malignant bone tumors.

Osteosarcoma. This is the most common malignant bone tumor with the exception of multiple myeloma. It is also the most common primary malignant bone tumor of childhood and adolescence. This tumor accounts for “0.2 percent of all malignant tumors in children” with an almost equal male to female occurrence rate.12 Osteosarcomas originate from bone forming mesenchymal cells and affect immature bone. Approximately 80 percent of these tumors form in the long, tubular bones with 40 percent of the lesions forming in the femur and 16 percent of the lesions occurring in the tibia.10

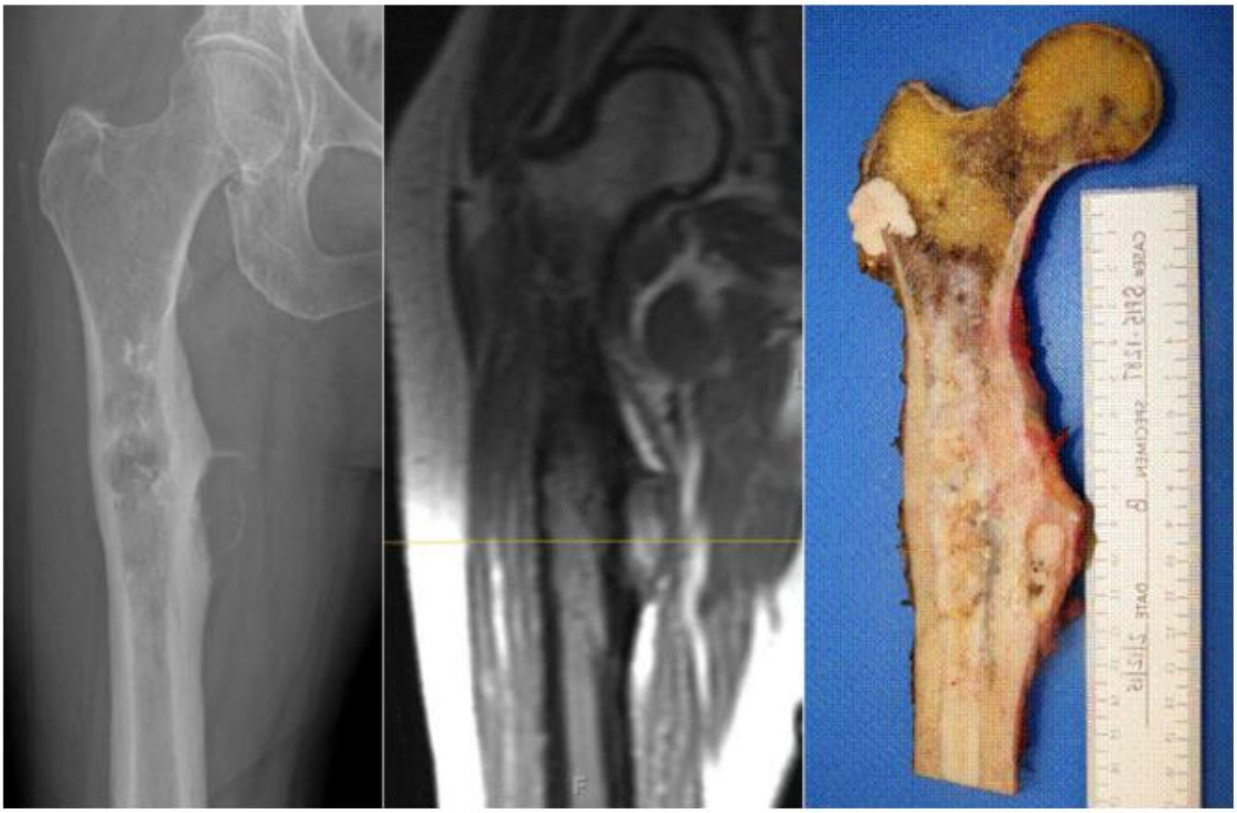

Figure 2: Malignant bone lesion in a 56-year-old man. Anteroposterior radiograph of the proximal right femur demonstrates a geographic, but poorly marginated lytic medullary lesion with chondroid mineralization, moderate endosteal scalloping with medial cortical thickening, and elevation of the periosteum suggesting an extraosseous soft tissue mass. Coronal T1-weighted MRI demonstrates extent of medullary cavity involvement and confirms a medial extraosseous mass. Gross pathology specimen correlated with MRI-confirmed chondrosarcoma.

This malignancy is most common in the 10- to 25-year-old patient with a peak incidence in the second decade of life during adolescent growth.13 The lesion most frequently affects the metaphyseal region of bone due to accelerated bone growth during this phase in life. The clinical presentation typically involves pain over the affected area with possible complaints of swelling or even a palpable mass. It is also not unusual for these tumors to have an associated soft tissue mass with the lesion. Normal lab tests may yield increased alkaline phosphatase levels due to the tumor's bone production.

Radiographic findings common to this malignancy are a mixture of lytic and sclerotic lesions, and cortical bone destruction.13 Periosteal reactions are those associated with aggressive findings such as a sunburst reaction or Codman's triangle type reaction. The MRI demonstrates high T2 and STIR weighted imagery with low signal on T1 weighted views. Gadolinium administration aids in the enhancement of the tumor's signal intensity.10 Magnetic resonance imaging is also very valuable in assessing the spread of the aggressive tumor into the epiphysis and can aid in determining any neurovascular involvement.13

Ewing's sarcoma. The second most common malignancy of bone in childhood and adolescence is Ewing's sarcoma. These tumors are thought to be of neuroectodermal origin and are highly aggressive in nature. The peak incidence is at age 15 with approximately 90 percent of these neoplasms occurring between the ages of 5 and 30 years.10 Ewing's sarcomas are more common in males and occur almost exclusively in Caucasians.

The clinical presentation is very similar to osteosarcoma with pain being a common finding. In addition, swelling and weight loss can also occur. This tumor has a predilection for long bones of the lower extremity affecting the femur and tibia commonly in the metadiaphyseal region of bone.13 Plain radiographic findings of Ewing's sarcoma are very aggressive. These changes include osteolysis of bone with cortical erosions and poor bone margins. These lesions demonstrate aggressive periosteal reactions such as onion peel and hair-on-end patterns. The MRI findings are very similar to osteosarcoma with low signal intensity on T1 imaging yet increased sensitivity on T2 and STIR images.13

Fibrosarcoma. This is a rare, malignant connective tissue tumor that occurs in the third to sixth decade of life. These tumors occur equally in males and females, and tend to be found in the metaphyseal region of long bones, which account for 70 percent of cases.10 Clinical findings in patients are complaints of pain and swelling with possible restriction of range of motion. Fibrosarcomas also have been known to extend into the epiphyseal region of bone and up to 80 percent of cases arise around the knee.10

The radiographic presentation is that of an aggressive bone lesion with typical bone destructive patterns. It is interesting to note that these lesions tend to have aggressive bone destruction with little to no periosteal reaction present.

Chondrosarcoma. Chondrosarcoma is a malignant, cartilage forming tumor that occurs during the third to sixth decade of life. These tumors occur more frequently in males with 45 percent of cases occurring in long bones with the femur being most common. These tumors are most commonly located in the metaphyseal region of bone but have been known to extend into the epiphysis as well. The clinical presentation includes symptoms of pain with the physical exam revealing a possible soft tissue mass. Additionally, up to 3 percent of patients can present with a pathological fracture.10

Chondrosarcomas are defined as being low- to high- grade tumors based on multiple radiographic findings. Low-grade tumors tend to have findings very similar to benign endochondromas and may be difficult to diagnose on radiographic, histologic and clinical exam.14 A plain radiographic exam can aid in the diagnosis of these tumors based on multiple findings. Typically, well organized calcifications and calcific "rings" within the tumor are indicative of a lower grade chondrosarcoma.10 In long tubular bones, the radiographic appearance of osteolysis and endosteal bone destruction with scattered calcification may be apparent. These radiographic appearance of these tumors can vary and may have outwardly aggressive features of bone destruction or slowly progressive findings.

What You Should Know About Benign Bone Tumors

As with malignant bone tumors, it is equally important to rely on clinical and radiographic findings in determining the most likely diagnosis for a bone lesion. Most benign bone lesions do not display aggressive bone destruction patterns or periosteal reactions similar to those of malignant lesions in the lower extremities. Therefore, the podiatric physician should be readily able to narrow down a differential diagnosis and determine the best course of action for the patient. The following are examples of common benign bone lesions found in the foot and lower extremities, and their characteristic radiographic findings.

Osteochondroma. The most common benign bone tumor, osteochondroma, accounts for up to 15 percent of all primary bone lesions.15 These tumors tend to occur between the first through third decades of life. These cartilage covered bony projections tend to occur in the metaphysis of long bones and involve the small bones of the hand or foot in 10 percent of cases.10

Clinical findings are usually that of a non-painful, slow growing mass. Radiographically, these bony protuberances tend to grow away from the nearby joint. Osteochondromas rarely have been noted to transform into chondrosarcomas with a very low incidence.15,16 The MRI findings demonstrate increased intensity on T2 weighted images and may be used to determine cartilage cap changes in cases of suspected malignancy.15 In the foot, a subungual exostosis is an osteochondromal type of lesion. Typically, this lesion occurs at the most dorsal aspect of the distal hallux with clinical patient findings of pain and swelling.

Enchondroma. An enchondroma is a benign hyaline cartilage tumor that occurs frequently in the hands and feet. These tumors have an equal male to female distribution, and occur between the first and third decades of life. Enchondromas tend to reside in the metaphyseal region of bone such as in the femur and tibia. In the hand and foot, these tumors may occur more in the diaphyseal region of bone. On very rare occasions, these tumors may transform into a chondrosarcoma. Radiographically, the lesion is a solitary, well marginated tumor, which may demonstrate endosteal cortical erosions. The MRI findings demonstrate a well-defined lesion with a high T2 signal intensity and low T1 signal intensity.10

Osteoid osteoma. This is a benign bone forming tumor that occurs more frequently in males between the first and second decades of life. The lesion is comprised of a core vascular tissue with an outer zone of bony sclerosis. The classic clinical presentation is that of night pain relieved with salicylates. These tumors primarily involve the diaphysis of long bones and are not infrequently found in the femur, tibia and bones of the foot. Radiographically, these lesions are radiolucent, cortical lesions that are surrounded by bony sclerosis and cortical thickening, and are usually less than 1 cm in diameter.

Osteoblastoma. A relatively benign bone tumor, the osteoblastoma can become aggressive and malignant. These tumors occur most commonly in males between the second and third decades of life. Patients clinically present with night pain that may or may not be relieved with salicylates. Osteoblastomas most frequently are localized in the diaphysis of long bones with 10 percent of cases located in the bones of the hands and feet.10

On plain radiographs, these lesions are expansile and osteolytic with bone sclerosis and periostitis present as well. However, the radiographic presentation makes diagnosis difficult and returning lesions may represent a malignant osteoblastoma.

Giant cell tumor. A giant cell tumor is an aggressive tumor that consists of connective tissue, stromal cells and giant cells. These tumors are more frequent in females between the fourth and fifth decades of life. Clinically, patients experience pain and swelling at the site of the lesion. These lesions are not uncommon in the lower extremities with 30 percent of cases involving the femur and 25 percent involving the tibia.10 The tumor may originate in the metaphysis but usually extends into the epiphyseal region of long bones.

On plain films, these expansive lesions tend to be osteolytic and extend into subchondral bone and display cortical thinning as well. The margins of the lesion can be either well or poorly defined, and tend to be quite large. Magnetic resonance images of lesions can help determine the extent of the lesion and demonstrate high T2 signal intensity.

Unicameral bone cyst. This is a benign tumor of unknown origin that occurs more frequently in males between the first and second decades of life. These lesions are usually asymptomatic in nature and are typically discovered after a pathological fracture.

In the lower extremity, these tumors are located in the metaphyseal region of long tubular bones of the femur and tibia, and are fluid filled. Lesions in patients over 20 years of age tend to be located in the innominate bone and the calcaneus. Plain radiographs of these lesions demonstrate a radiolucent, centrally located tumor with cortical thinning and some osseous expansion.10

Calcaneal lesions are usually well defined and located in the neutral triangle of the bone. The fallen fragment sign is typical with pathological fractures and represents a fragment of fractured bone “floating” to the dependent aspect of the cyst.

In Conclusion

Bone tumors can be a challenge to even the most experienced radiologist or oncologist. The key to differentiating the benign from the aggressive and potentially malignant lesion is to understand the basic radiographic differences between the two. The podiatric physician should be able to narrow down the differential diagnosis based on the patient’s clinical findings, age, the lesion’s location in the bone and the radiographic appearance of the tumor.

After ascertaining this, the physician can determine the best course of action to give the patient the best possible prognosis. If necessary, a surgeon experienced with the treatment of these tumors may obtain a bone biopsy to help determine an accurate diagnosis and treatment regimen.

No Conflict of interest.

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