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Imaging of bone tumors for the musculoskeletal oncologic surgeon

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ABSTRACT

The appropriate diagnosis and treatment of bone tumors requires close collaboration between different medical specialists. Imaging plays a key role throughout the process. Radiographic detection of a bone tumor is usually not challenging. Accurate diagnosis is often possible from physical examination, history, and standard radiographs. The location of the lesion in the bone and the skeleton, its size and margins, the presence and type of periosteal reaction, and any mineralization all help determine diagnosis. Other imaging modalities contribute to the formation of a diagnosis but are more critical for staging, evaluation of response to treatment, surgical planning, and follow-up.When necessary, biopsy is often radioguided, and should be performed in consultation with the surgeon performing the definitive operative procedure. CT is optimal for characterization of the bone involvement and for evaluation of pulmonary metastases. MRI is highly accurate in determining the intraosseous extent of tumor and for assessing soft tissue, joint, and vascular involvement. FDG-PET imaging is becoming increasingly useful for the staging of tumors, assessing response to neoadjuvant treatment, and detecting relapses.Refinement of these and other imaging modalities and the development of new technologies such as image fusion for computer-navigated bone tumor surgery will help surgeons produce a detailed and reliable preoperative plan, especially in challenging sites such as the pelvis and spine.

1. Introduction

Advances in medical imaging over the last two decades have greatly impacted the management of musculoskeletal tumors. In general, the imaging of musculoskeletal neoplasms can be considered from several standpoints: detection of pathology, diagnosis, staging, evaluation of treatment, planning of surgery, and follow-up.

2. Detection of pathology

Radiographic detection of a bone tumor is usually not challenging and may occur incidentally or in an effort to elucidate the cause of a clinical complaint. Despite the advances in imaging technology that have occurred in recent decades, especially the introduction of cross-sectional imaging modalities, such as computed tomography (CT) and magnetic resonance imaging (MRI), plain radiographs remain the key in the initial detection of a bone lesion [1]. Occasionally, however, small lesions such as osteoid osteoma or large lesions with subtle bone destruction such as Ewing's sarcoma and lymphoma may be difficult to locate in this manner.

When plain radiographs are normal, a technetium bone scan is often helpful in revealing an osseous lesion. It is non-specific but highly sensitive and allows for the evaluation of the entire skeleton. Positron emission tomography using fluorodeoxy-glucose (FDG-PET) has been shown to be more sensitive than CT, MRI, and scintigraphy in detecting primary and metastatic tumors, however, it is relatively nonspecific because FDG may also accumulate in reactive and inflammatory lesions [1].

3. Diagnosis

The age of the patient is the single most important piece of clinical information that can be used in conjunction with radiographic findings to establish a diagnosis [1]. Standard radiographs are the single most important imaging diagnostic modality. They reveal the most useful information about location, size, and morphology, including periosteal reaction and matrix of the lesion (calcifications and/or ossifications) [1,2]. Based on a patient's medical history, physical examination, and plain radiographs, the diagnosis of a bone tumor can be established in over 80% of cases [3].

The location of the lesion within the skeleton and within the involved bone(s) has a major impact on differential diagnosis

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[1,2]. Most primary bone tumors arise in the metaphysis, but some neoplasms like chondroblastoma, giant cell tumor, and clear cell chondrosarcoma are often epiphyseal. Ewing's sarcoma usually originates in the diaphysis of long tubular bones or in flat bones, such as the pelvis. Osteo-fibrous dysplasia occurs in long bones, commonly involves the diaphysis, and it has specific preference for the tibia, as does adamantinoma. Periosteal osteosarcoma is another tumor with a propensity for diaphyseal origin, and unlike conventional osteosarcoma, arises on the surface of the involved bone. Parosteal osteosarcoma is often found on the posterior aspect of the distal femur. Simple bone cysts, enchondromas, and fibrous dysplasia are almost always centrally located in the bone, whereas an eccentric location is characteristically observed with aneurysmal bone cysts, chondromyxoid fibroma, and non-ossifying fibroma [1]. Others tumors, such as osteoid osteoma and eosinophilic granuloma, appear to have no anatomic predilection [1,2].

The size of a lesion is both diagnostic and prognostic. Some lesions tend to have a more spherical shape, like giant cell tumor and osteosarcoma; others tend to conform to the shape of the bone in which they arise, like chondrosarcoma [1].

The radiographic margins of a lesion provide most of the information regarding its rate of growth, an important indicator as to whether it is benign or malignant. Four types of lesions are encountered: static, slow-growing, faster-growing, and the fastest lesions [4]. Static lesions have a solid sclerotic (radiodense) boundary between the periphery of the tumor and the adjacent host bone. Slow tumors are characterized by sharp demarcation between the tumor and host bone, without sclerosis at the periphery of the lesion, thereby producing a "geographic" pattern of destruction. Faster growth results in the "moth-eaten-pattern", such in Ewing's sarcoma, and the fastest growing lesions reveal an ill-defined region between tumor and host bone ("permeative bone destruction"), such as is observed with conventional osteosarcoma. Benign lesions, characterized by low biologic activity, usually exhibit well-defined borders, with or without sclerosis. Indistinct margins are typical of aggressive lesions with greater biologic activity [1,2], as is often seen with malignancy.

Like the margins of the lesion, the periosteal reaction is an indicator of biologic activity. An uninterrupted, smooth periosteal reaction usually indicates a slow-growing, benign lesion. A disrupted periosteal proliferation is often seen in bone sarcomas. There are several types of periosteal reaction: amorphous (thick), laminated ("onion-skin") and spiculated ("sunburst"). Of these, only the first type is indicative of a relatively slow, often benign, process [1,2]. When a rapidly growing tumor breaks through the cortex and destroys the newly formed periosteal laminated bone, remnants of the latter at the tumor borders form a Codman's triangle [1].

Analysis of any internal mineralization may help to characterize the intercellular material produced by the lesion. The matrices produced by mesenchymal cells include: osteoid, bone, chondroid, myxoid, and fibrous tissue. The tumor matrix provides useful means of differentiating osteoblastic from chondroblastic processes. In a typical osteoblastic lesion, ossified matrix may appear as radiographically dense lumps or clouds with fuzzy or sharp margins. A chondroid matrix directs one toward a chondroblastic process; this matrix may appear as rings or arcs that represent enchondral ossification along lobules of cartilage. Calcifications may take the form of stippled or flocculent deposits of calcium or bone in the lesion. In general, chondroid matrix mineralizes in more mature and well-differentiated lesions [1,2]. Matrix mineralization is absent in many lesions, such as Ewing's sarcoma.

In general, how the tumor affects the bone is best appreciated on initial radiographs. Anatomic details of the lesions are further delineated on CT and MRI, yet these studies yield little information the biologic activity of the tumor. CT is superior to MRI in the detection and characterization of matrix mineralization (osteoid or chondroid), cortical involvement, and periosteal reaction [5]. It is particularly helpful in evaluating bone lesions that are difficult to see clearly on radiographs, either because of the nature of the lesion or because of the bone involved, such as the scapula, pelvis, or sacrum [1]. CT should be performed on a helical scanner that enables improved two-dimensional images and three-dimensional reconstruction capability [3]. Multiplanar cuts are useful for the diagnosis of lesions localized to cortical bone, such as osteoid osteomas, Langerhans' cell histiocytosis, and Brodie's abscesses [5]. MRI can also be helpful in the evaluation of tumor matrix. The complementary use of different pulse sequences facilitates tissue characterization and can, in some instances, allow a specific diagnosis [6].

The evaluation of tumor margins may be less clear on CT or MRI as both benign and malignant lesions often have a fibrous pseudocapsule. Radiographs may therefore provide easier evaluation regarding margins [5]. However, bone marrow edema in the setting of a variety of lesions may be appreciated on MRI where it is not apparent on other imaging modalities. The extent of marrow involvement by the tumor is often best delineated on T1-weighted sequences, with surrounding edema better demonstrated on fat-saturated T2-weighted or STIR sequences. In establishing a differential diagnosis, one must be aware of those lesions commonly associated with significant bone marrow edema [6]; benign lesions may demonstrate more surrounding marrow edema than malignancies. For example, the "flare phenomena" is found in osteoid osteoma, osteoblastoma, chondroblastoma, and eosinophilic granuloma; the large inflammatory response of the surrounding soft tissues simulates a more aggressive tumor. Extensive marrow edema surrounding a relatively small lesion is often seen with benign tumors, inflammatory lesions, and stress fractures. Minimal edema surrounding a large lesion is more likely associated with malignancy, but not necessarily; primary bone malignancies such as osteosarcoma, Ewing's sarcoma, and chondrosarcoma may also have associated bone marrow edema [6].

Triple-phase bone scintigraphy is helpful in the evaluation of primary bone tumors. Dynamic images define the aggressiveness of these lesions. Delayed-phase images are relatively non-specific; increased radiotracer uptake is seen wherever new bone is being formed. Therefore, a positive scan may result from both malignant and benign processes, including infection, fracture, and inflammation. For lesions such as plasmacytoma, multiple myeloma, and occasionally in chordoma, false negative "cold" technetium bone scans have been reported.

PET imaging differs considerably from conventional imaging modalities such as radiography, CT, and MRI, as it quantifies the biologic activity of tissue via the use of a labeled glucose analog, fluorodeoxyglucose (FDG) [^{18}F], however, it does not quantify morphologic abnormality. FDG-PET has been proposed for discriminating between benign and malignant osseous lesions and in the grading of sarcomas [7]. In addition to histopathologic grade, this modality has also demonstrated correlation with the cellularity, mitotic activity, and over-expression of p53 in bone sarcomas [7]. In this sense, the metabolic data acquired by FDG-PET may have prognostic value in the sarcoma setting [8].

After a differential diagnosis has been established, one must ask whether a biopsy is necessary. Some lesions are readily identifiable on imaging or the differential is sufficiently narrow to allow for the next step in management to be made: to monitor the lesion radiographically over time or to proceed directly with appropriate treatment. However, in cases where the differential is broad and/or where a precise diagnosis is critical for further management decisions, microscopic analysis is the final and most important