Conditions Simulating Primary Bone Neoplasms

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KEYWORDS

• Osteonecrosis • Osteomyelitis • Sarcoidosis • Subchondral cyst • Amyloidosis
• Heterotopic ossification • Stress fracture

ABSTRACT

A number of nonneoplastic conditions can mimic tumors of bone. Some of the more common mimics of primary bone tumors include infectious, inflammatory, periosteal, and degenerative joint disease-associated lesions that produce tumorlike bone surface-based or intraosseous lesions. This article considers a spectrum of reactive and nonreactive processes including stress fracture, subchondral cysts, osteonecrosis, heterotopic ossification, osteomyelitis, sarcoidosis, and amyloidoma that can present in such a way that they are mistaken for a tumor arising primary in bone.

OVERVIEW

Conditions simulating primary bone neoplasms are encountered on a regular basis by those caring for patients with musculoskeletal abnormalities. In many of these scenarios, lesions with classic radiologic and clinical findings typically pose little diagnostic or patient management challenges. In contrast, lesions with unusual or inconclusive radiologic features are biopsied to exclude neoplasm. In these situations, the most common pitfall for the pathologist is to under-recognize the non-neoplastic lesional tissue and misinterpret the biopsy as nondiagnostic, leading to an unnecessary repeat biopsy. Alternatively, the lesion may be surgically removed without a preoperative diagnosis, and the pathologist runs into diagnostic difficulties by assuming it represents a neoplasm. These pitfalls can be avoided by gaining a better understanding of the histologic, clinical, and radiologic features of these non-neoplastic mimics.

STRESS FRACTURES

Stress fractures are subclassified into fatigue fractures caused by excessive, repetitive load bearing onto normal bone (eg, long-distance running) and insufficiency fractures, caused by normal load bearing upon structurally compromised bone (eg, osteoporotic bone). Unlike pathologic fractures, this terminology generally refers to bones that are not involved by tumor.

Key Points
Stress Fracture

- Subclassification includes 2 types—fatigue and insufficiency
- Affected bones are not involved by tumor
- Radiologic findings can mimic benign and malignant tumors. MRI (correlating T1- and T2-weighted images) is most helpful in making the distinction
- Histologic findings vary with lesional age. Early lesions—woven bone, immature cartilage, myofibroblastic cell proliferation, and fibrovascular tissue. More mature lesions—longer interconnecting trabeculae of woven bone with osteoblastic rimming.
- Can be mistaken for osteosarcoma, but lacks the disorganized growth pattern, cytologic atypia, and lace-like osteoid matrix seen in osteosarcoma.

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RADIOLOGIC FEATURES

Plain radiographs may demonstrate a visible fracture line, or localized osteopenia, periosteal reaction, sclerosis, or callus formation depending on the stage of healing at the time of presentation. These features are better demonstrated on computed tomography (CT), particularly in locations such as the pelvis and sacrum that are difficult to evaluate on radiographs given overlying structures. MRI is a highly sensitive and specific imaging tool for making the diagnosis of a stress fracture. It is critical to correlate the T1- and fluid-sensitive T2-weighted images, since the signal abnormality is frequently exaggerated on T2 and disproportionate to the findings on T1 images. Stress fractures can be confused with many benign and malignant processes in the bone, including osteomyelitis, metastases, and primary sarcoma. However, all of the other entities can usually be distinguished from stress fracture on MRI since they all result in confluent replacement of the marrow fat signal on T1-weighted images (**Fig. 1**).

MICROSCOPIC FEATURES

The histologic features of stress fracture depend on the chronologic age of the fracture and the degree of structural compromise to the bone. Following fracture, there may be an initial inflammatory component, followed by woven bone formation and then a chronic phase of bone remodeling (**Fig. 2**).[1] The abnormality is characterized by only minimal callus formation. Small biopsies of these fractures can be challenging to diagnose, and the most important pitfall for the pathologist is to not recognize that lesional tissue, albeit non-neoplastic tissue with reactive changes, is present in the biopsy. Tissue received in the later stages of healing shows a more organized pattern created by interconnected trabeculae of immature bone rimmed by osteoblasts.

DIFFERENTIAL DIAGNOSIS

Stress fractures, composed of abundant woven bone surrounded by a bland spindle cell stroma, bring fibrous dysplasia and low-grade osteosarcoma into the differential diagnosis. The distinction can be made by recognizing a reactive loose, fibrovascular proliferation containing slender, myofibroblastic spindled cells and several thin-walled dilated blood vessels in the setting of a fracture.[2] This contrasts with fibrous dysplasia, in which the cells contain oval- to spindle-shaped nuclei embedded in a more collagen-rich stroma containing only scattered thin-walled blood vessels. Once again, radiologic correlation is important, because the imaging features of fibrous dysplasia and low-grade osteosarcoma do not resemble those of a stress fracture.

When imaging findings of a stress fracture lead radiologists to be worried about a high-grade sarcoma such as Ewing sarcoma or osteosarcoma, pathologists can help avoid unnecessary repeat biopsy by recognizing the reactive histologic findings devoid of cytologic atypia, and thus suggest the possibility of a stress fracture. In these situations, it is important to be sure the biopsy tissue clearly represents the radiologic abnormality in question.

SUBCHONDRAL (SUBARTICULAR) CYSTS

Subchondral cysts refer to a group of non-neoplastic, intraosseous cysts located immediately below the articular cartilage. They occur in the setting of osteoarthritis, most commonly in degenerative joint disease (osteoarthritic cyst), but occasionally in inflammatory arthritides such as rheumatoid arthritis. These cysts are often referred to as geodes by radiologists and surgeons. Subchondral cysts may also arise as a result of trauma (post-traumatic cysts).

Intraosseous ganglion cysts are another type of subchondral cyst that can mimic a primary bone tumor. Intraosseous ganglia often present as incidentally detected juxta-articular lesions in asymptomatic adult patients. Unlike a true synovial cyst, they do not have a connection with adjacent synovial structures. They most often involve the subchondral aspect of bones in the regions of the foot and ankle, knee and hip.[3–5]

Key Points
Subchondral Cysts

- Subclassification includes degenerative (osteoarthritic) and intraossesous ganglion cysts.
- They are located immediately below articular cartilage.
- Unlike intraosseous ganglions, radiologic features of advanced degenerative joint disease are always seen with osteoarthritic cysts.
- Imaging features of large cysts can be mistaken for epiphyseal-based primary bone tumors.
- Histologically, subchondral cysts contain loose myxoid material surrounded by a fibrous cyst wall.